The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 233

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

DAVID A. FISCHHOFF and STEPHEN G. ROGERS

Original Junior Party,

v.

MICHAEL J. ADANG and JOHN D. KEMP

Original Senior Party.

Interference 103,324

FINAL HEARING: April 27, 2000

Before SCHAFER, GRON, and LEE, Administrative Patent Judges.

PER CURIAM

Interference 103,324

FINAL DECISION

1. Background

September 26, 1983 - Michael J. Adang and John D. Kemp (hereafter Adang) filed U.S. Patent Application (Application) 06/535,354, entitled "INSECT RESISTANT PLANTS" (hereafter Adang '83).

April 4, 1986 - Adang filed continuation-in-part Application 06/848,733 (hereafter Adang '86), claiming benefit under 35 U.S.C. § 120 of the September 26, 1983, filing date of Adang '83.

November 20, 1986 - David A. Fischhoff and Stephen G. Rogers (hereafter Fischhoff) filed Application 06/932,818, entitled "INSECT RESISTANT TOMATO PLANTS" (hereafter Fischhoff '86).

October 21, 1988 - Adang filed continuation-in-part Application 07/260,574 (hereafter Adang '88), claiming benefit under 35 U.S.C. § 120 of the April 4, 1986, filing date of Adang '86, and the September 26, 1983, filing date of Adang '83.

June 10, 1991 - Adang filed continuing Application 07/713,624 (Adang's involved application)(hereafter Adang '91), claiming benefit under 35 U.S.C. § 120 of the October 21, 1988, filing date of Adang '88, the April 4, 1986, filing date of Adang '86, and the September 26, 1983, filing date of Adang '83.

Interference 103,324

November 26, 1991 - The Board of Patent Appeals and Interferences (Board) entered its decision in ex parte Appeal No. 91-0967 (Appendix A). Therein the Board affirmed an examiner's final rejection of Claims 1-9 and 37 of Fischhoff '86, under 35 U.S.C. § 103 in view of the combined teachings of European Patent Application 193,259, published September 3, 1986 (DeGreve); Caplan et al. (Caplan), "Introduction of Genetic Material into Plant Cells," Science, Vol. 22, pp. 815-21 (1983); Schnepf et al. (Schnepf '036), U.S. Patent 4,467,036, patented August 21, 1984; Schnepf et al. (Schnepf), "The Amino Acid Sequence of a Crystal Protein from Bacillus thuringiensis Deduced from the DNA Base Sequence," The Journal of Biological Chemistry, Vol. 260, No. 10, pp. 6264-272 (1985); and Adang et al. (Adang Gene), "Characterized Full-Length and Truncated Plasmid Clones of the Crystal Protein of Bacillus thuringiensis subsp. Kurstaki-HD-73 and their Toxicity to Manduca Secta," Gene, Vol. 36, pp. 289-300 (1985). The patentability of all claims stood or fell with independent Claim 1. See Decision on Appeal No. 91-0967, p. 6 ("these claims stand or fall based on limitations in independent claim 1"). Claim 1 of Appeal No. 91-0967 read (Decision on Appeal No. 91-0967, pp. 1-2):

1. A method of producing genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larvae which comprises:

(a) inserting into the genome of a tomato cell a chimeric gene which comprises

(I) a promoter which functions in plants to cause the production of a mRNA transcript;

(ii) a coding sequence that causes the production of mRNA encoding a crystal protein toxin of Bacillus thuringiensis; and

(iii) a 3' non-translated region which functions in tomato to cause the addition of polyadenylate nucleotides to the 3' end of the mRNA;

(b) selecting transformed tomato cells; and

(c) regenerating from the transformed tomato cells genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larve.

In the same decision, the Board reversed an examiner's rejection of Claims 1, 2, 6, and 37 of Fischhoff '86 under 35 U.S.C. § 112, first paragraph, as nonenabled by its supporting specification. The Board was not convinced by Vaeck et al. (Vaeck), "Transgenic Plants Protected from Insect Attack," Nature, Vol. 328, pp. 33-37 (1987), or Barton et al. (Barton), "Bacillus thuringiensis δ-Endotoxin Expressed in Transgenic Vicotiana tabacum Provides

Resistance to Lepidopteran Insects," Plant Physiology, Vol. 85, pp. 1103-109 (1987), that the § 112 rejections were justified.

December 23, 1991 - Fischhoff filed continuing Application 07/813,250 (Fischhoff's involved application)(hereafter Fischhoff '91), claiming benefit under 35 U.S.C. § 120 of the November 20, 1986, filing date of Fischhoff '86.

February 28, 1994 - An Administrative Patent Judge (APJ) declared Interference 103,324 between subject matter claimed in Fischhoff '91, and Adang '91. Count 1 (Paper No. 2) is reproduced below:

Count 1

> A tomato plant which has been regenerated from a tomato plant cell transformed to comprise a full length Bacillus thuringiensis crystal protein gene capable of encoding a Bacillus thuringiensis crystal protein of about 130 kD under control of a promoter such that said gene is expressible in said plant in amounts insecticidal to Lepidopteran insects.

For the subject matter of Count 1, the APJ accorded:

Adang benefit of the October 21, 1988, filing date of Adang '88, and the April 4, 1986, filing date of Adang '86; and

Fischhoff benefit of the November 20, 1986, filing date of Fischhoff '86.

The APJ indicated that the following claims of the parties correspond to Count 1:

Fischhoff: Claims 11, 12, 15, 16, 20, 21, 24, 25, 38, 39, 42, and 43;

Adang: Claims 16, 17, 22, 25-27, 29-32, 34, 46-50, 57, 40 (dependent upon Claims 16, 26, 27, 29, or 30), and 43 (dependent upon Claims 16, 26, 27, 29, or 30).

2. Motions

The following motions are before us for final hearing:[1]

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[1] The parties filed the following additional motions which were deferred, denied, or dismissed by an Administrative Patent Judge (APJ)(Paper No. 121) but not raised in the principal briefs for review at final hearing. Thus, the parties have waived consideration of the motions (37 CFR §§ 1.640(b) and 1.658(a)):

Fischhoff's motion 4 (Paper No. 38) for judgement under 37 CFR § 1.633(a) that Adang's Claims 16, 22, 25-27, 29-32, 40/16, 40/26, 40/27, 40/29, 40/30, 43/16, 43/26, 43/27, 43/29, 43/30, 46/16, 46/26 and 47-50 are unpatentable under 35 U.S.C. § 102 and/or § 103 (deferred (Paper No. 121));

Fischhoff's contingent motion 5 (Paper No. 39) for judgement under 37 CFR § 1.633(a) that Adang's Claims 15, 24, 42/16, 42/26, 42/27, 42/29, 42/30, 44/16, 44/26, 44/27, 44/29 and 44/30 are unpatentable under 35 U.S.C. § 102 and/or § 103 (deferred (Paper No. 121));

Fischhoff's motion 6 (Paper No. 40) for judgment under 37 CFR § 1.633(a) that Adang's Claims 16, 22, 25-27, 29-32, 40/16, 40/26, 40/27, 40/29, 40/30, 43/16, 43/26, 43/27, 43/29, 43/30, 46/16, 46/26 and 47-50 are unpatentable under 35 U.S.C. § 101 (deferred (Paper No. 121));

Fischhoff's contingent motion 7 (Paper No. 41) for judgment under 37 CFR § 1.633(a) that Adang's Claims 15, 24,

(continued...)

[1](...continued)
42/16, 42/26, 42/27, 42/29, 42/30, 44/16, 44/26, 44/27, 44/29 and 44/30 are unpatentable under 35 U.S.C. § 101 (deferred (Paper No. 121));

Fischhoff's motion 8 (Paper No. 20) under 37 CFR § 1.633(a) for judgment that Adang violated 37 CFR § 1.56 (deferred (Paper No. 121));

Fischhoff's motion 9 (Paper No. 21) for discovery under 37 CFR § 1.687 (denied (Paper No. 121));

Fischhoff's motion 10 (Paper No. 22) for testimony and discovery under 37 CFR § 1.671(g)(denied (Paper No. 121));

Fischhoff's contingent motion 12 (Paper No. 24) for judgment under 37 CFR § 1.633(a) that Claims 17, 34, and 57 are unpatentable under 35 U.S.C. § 102 (dismissed (Paper No. 121));

Adang's motion 4 (Paper No. 18) under 37 CFR § 1.633(c) to redefine the interfering subject matter by substituting a broader count, adding claims 68 and 69 to Adang's application, and adding claims 44 and 45 to Fischhoff's application and Adang's motion under 37 CFR § 1.633(f) to be accorded benefit of three prior applications (deferred (Paper No. 121)). Adang explicitly states (AB, p. 5, first full para.; emphasis added):

> In Fischhoff's Brief for Final Hearing, Fischhoff limits its earliest alleged date for the conception and actual reduction to practice to June 27, 1986. These alleged facts, even if accepted at face-value, do not antedate Adang's actual and constructive reductions to practice of tomato plants within the scope of the Count. In view of these facts it is not necessary for Adang to rely upon its earliest and/or best evidence to prevail in this Interference. Therefore, Adang will not maintain its position that the Count needs to be broadened.[;]

(continued...)

A. Fischhoff's Motions

Fischhoff's motion 1 (Paper No. 35) under 37 CFR § 1.633(c)(3) to designate Adang's Claims 15, 24, 42/16, 42/26, 42/27, 42/29, 42/30, 44/16, 44/26, 44/27, 44/29, and 44/30 as corresponding to the count (denied (Paper No. 121));

Fischhoff's motion 2 (Paper No. 36) for judgment under 37 CFR § 1.633(a) that Adang's Claims 16, 22, 25-27, 29-32, 40/16, 40/26, 40/27, 40/29, 40/30, 43/16, 43/26, 43/27, 43/29, 43/30, 46/16, 46/26 and 47-50 are unpatentable under 35 U.S.C. § 112 (deferred (Paper No. 121));

Fischhoff's contingent motion 3 (Paper No. 37) for judgment under 37 CFR § 1.633(a) that Adang's Claims 15, 24, 42/16, 42/26, 42/27, 42/29, 42/30, 44/16, 44/26, 44/27, 44/29 and 44/30 are unpatentable under 35 U.S.C. § 112 (dismissed as Fischhoff motion 1 was denied (Paper No. 121); renewed at Final Hearing as Fischhoff motion 1 has been granted (37 CFR § 1.656(b));

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[1](...continued)

Adang's contingent motion 5 (Paper No. 19) under 37 CFR § 1.633(a) for judgment that Fischhoff's claims to be added are not patentable to Fischhoff under 35 U.S.C. § 102 or § 103 (dismissed (Paper No. 121)); and

Adang's contingent motion 6 (Paper No. 65) under 37 CFR § 1.635 to be accorded a testimony period to provide evidence in opposition to Fischhoff's motions 2, 3, 6, 7, 8 and 11 under 37 CFR § 1.639(c)(dismissed (Paper No. 121)).

Fischhoff's motion 11 (Paper No. 23) under 37 CFR § 1.633(g) to attack the benefit accorded Adang of the April 4, 1986, filing date of Adang '86 (deferred (Paper No. 121)):

Fischhoff's motion 13 (Paper No. 25) under 37 CFR § 1.633(c)(2) to add new Claims 44, 45, and 46 [(Appendix B)] and have the new claims designated as corresponding to the count (denied (Paper No. 121));

Fischhoff's contingent motion 14 (Paper No. 26) under 37 CFR § 1.633(f) for benefit of the November 20, 1986, filing date of Fischhoff '86 for new Claims 44, 45, and 46 (dismissed as Fischhoff motion 13 was denied (Paper No. 121); renewable at Final Hearing if Fischhoff motion 13 is granted (37 CFR § 1.656(b)); and

Fischhoff's motion 15 (Paper No. 214) to suppress evidence under 37 CFR § 1.656(h).

B. Adang's Motions

Adang's motion 1 (Paper No. 15) under 37 CFR §1.633(f) to be accorded benefit of the September 26, 1983, filing date of Adang '83 (deferred (Paper No. 121));

Adang's motion 2 (Paper No. 16) under 37 CFR § 1.633(a) for judgment that Fischhoff's claims corresponding to the count are

not patentable to Fischhoff under 35 U.S.C. § 102 and/or § 103 (deferred (Paper No. 121)); and

Adang's motion 3 (Paper No. 17) under 37 CFR § 1.635 to disclose or disregard unintentional and harmless omissions from Examples 3 and 4 of Adang's applications (deferred (Paper No. 121)).

3. Count construction

Preliminary construction of interference Count 1 is outcome-determinative of many of the issues presented by this interference. Construction of the count is a matter of law. Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 500, 42 USPQ2d 1608, 1612 (Fed. Cir. 1997); DeGeorge v. Bernier, 768 F.2d 1318, 1321, 226 USPQ 758, 760 (Fed. Cir. 1985).

> Interference counts are given the broadest reasonable interpretation possible, and resort to the specification is necessary only when there are ambiguities inherent in the claim language or obvious from arguments of counsel. . . . If there is such ambiguity, resort must be had to the specification of the patent from which the copied claim came.

Id. at 1321-22, 226 USPQ at 760-61.

As we read Count 1, it is drawn to tomato plants that have been regenerated from tomato plant cells transformed by particular genetic constructs. The transformed tomato plant

cells from which the new tomato plants are regenerated are conventional tomato plant cells which have been transformed by a "full length Bacillus thuringiensis crystal protein gene" which encodes "a Bacillus thuringiensis crystal protein of about 130 kD[,] under control of a promoter" which directs expression of full length Bacillus thuringiensis (Bt) crystal protein gene and production of 130 kD Bt crystal protein "in amounts insecticidal to Lepidopteran insects" (Count 1).

To understand the full scope of the new tomato plants defined by Count 1, we first look at the language of the count as a whole. Genentech, Inc. v. Chiron Corp., 112 F.3d at 500, 42 USPQ2d at 1612. The full length Bt crystal protein gene to which Count 1 refers encodes a Bt crystal protein which (1) must have a molecular weight of "about 130 kD", and (2) must be insecticidal to Lepidopteran larvae in the amounts produced by tomato plants regenerated from cells transformed by the full length Bt crystal protein gene.

Adang's specifications teach that the ~130 kD molecular weight limitation in Count 1 refers to a Bt crystal protein protoxin and not to a lower molecular weight Bt crystal protein toxin which may either be (1) encoded by a truncated form of the full length Bt crystal protein gene, or (2) activated and/or

cleaved from the protoxin in the gut of Lepidopteran insects. Adang '83 and Adang '86, pages 1 and 2, first and second paragraphs under BACKGROUND Insecticidal Protein of each application, teach that a full length Bt crystal protein gene is readily distinguished from a truncated form of the full length Bt crystal protein gene by the molecular weight of the Bt crystal protein each encodes and its toxicity toward Lepidopteran larvae before and after consumption by Lepidopteran insects (id.):

> Bacillus thuringiensis, a species of bacteria closely related to B. cereus, forms a proteinaceous crystalline inclusion during sporulation. This crystal is parasporal, forming within the cell at the end opposite from the developing spore. The crystal protein, often referred to as w-endotoxin, has two forms: a nontoxic protoxin of approximate molecular weight (MW) of 130 kilodaltons (kD), and a toxin having an appox. MW of 67 kD. The crystal contains the protoxin protein which is activated in the gut of larvae of a number of insect species. . . . [S]olubilized protoxin from B. thuringiensis var. israelensis is toxic to Aedes aegypti adults. During activation, the protoxin is cleaved into two polypeptides, one or both of which are toxic. In vivo, the crystal is activated by being solubilized and converted to toxic form by the alkalinity and proteases of the gut. . . .
>
> B. thuringiensis and its crystalline endotoxin are useful because the crystal protein is an insecticidal protein known to be poisonous to the larvae of over a hundred of species of insects, most commonly those from the orders Lepidoptera and Diptera. . . .

Fischhoff's specifications also teach that full length and truncated Bt crystal protein genes may be distinguished by the

molecular weight and toxicity of the Bt crystal protein each encodes. For example, Fischhoff '86 teaches (p. 1, para. 1):

> Bacillus thuringiensis is a spore forming soil bacterium which is known for its ability to produce a parasporal crystal protein which is toxic to a wide variety of Lepidopteran larvae. The crystals, which account for about 20-30% of the dry weight of the sporulated cultures, consist primarily of a single, high molecular weight protein (~134 kilodaltons (KD)) which is produced only during sporulation. The crystal protein is produced in the bacterium as the protoxin which is activated in the gut of susceptible larvae to produce a toxic protein having a molecular weight of about 67 KD.

Considering Count 1 as a whole, we conclude that it is directed to tomato plants which have been regenerated from tomato plant cells transformed by a full length Bt crystal protein gene which encodes a Bt crystal protein having a molecular weight of ~130 kD. Therefore, the tomato plants encompassed by Count 1 are prima facie distinct from tomato plants which have been regenerated from tomato plant cells transformed by truncated Bt crystal protein genes which encode Bt crystal proteins having a molecular weight substantially less than ~130 kD, e.g., an active toxin with a molecular weight of at least ~67 kD, but substantially less than ~130 kD. The molecular weight of ~130 kD is the molecular weight attributed to unactivated Bt crystal protein protoxin.

As we construe the language of Count 1, "full length . . . gene" refers to a genetic sequence which encodes a Bt crystal protein having a molecular weight of about 130 kD. On the other hand, the term "truncated" is used throughout the parties' respective specifications in reference to genetic sequences which encode Bt proteins with molecular weights of substantially less than ~130 kD. The specifications of Adang '83 and Adang '86, page 3 of each, expressly state that the "full-size . . . protoxin" has a molecular weight of ~130 kD. At page 5 of his specification, Fischhoff states (Fischhoff '86, spec., p. 5, lines 26-32):

> Hence, for purposes of the present invention by "toxin protein" is meant either the full-length toxin as naturally produced by Bacillus thuringiensis or fragments thereof ("truncated toxin") possessing insecticidal activity toward the aforementioned Lepidopteran larvae.

The control promoter to which Count 1 refers is defined in terms of the amount of Bt crystal protein of about 130 kD which is produced by the claimed tomato plants. So defined, the control promoter sequence must not only direct expression of the full length Bt crystal protein gene in tomato plants regenerated from tomato plant cells genetically transformed to produce Bt crystal protein of about 130 kD, but also must direct the

regenerated tomato plants to produce Bt crystal protein of about 130 kD in amounts insecticidal to Lepidopteran insects (Count 1), i.e., the tomato plants must produce Bt crystal protein having a molecular weight of ~130 kD in amounts sufficient to destroy or control Lepidopteran insects.[2] Stated another way, if the tomato plants produce Bt crystal protein of about 130 kD in amounts sufficient to destroy or control Lepidopteran insects, the tomato plants are encompassed by Count 1. On the other hand, if tomato plants do not produce Bt crystal protein of about 130 kD or produce Bt crystal protein of about 130 kD but in amounts insufficient to destroy or control Lepidopteran insects, the tomato plants are not encompassed by Count 1.

The phrase "amounts insecticidal to Lepidopteran insects" means amounts which destroy or control Lepidopteran insects (see footnote 2). Persons having ordinary skill in the art immediately would have understood the inherent relative nature of the limitation. For example, Fischhoff states (Fischhoff '86, p. 4, lines 21-28; emphasis added):

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[2] According to Webster's New Collegiate Dictionary, G. & C. Merriam Company, Springfield, Mass., p. 597 (1976), the word "insecticidal" means "destroying or controlling insects."

> The promoter selected should be capable of causing sufficient expression to result in the production of an effective amount of toxin protein to render the plant toxic to Lepidopteran larvae. Those skilled in the art recognize that the amount of toxin protein needed to induce the desired toxicity may vary with the particular Lepidopteran larvae to be protected against.

Adang similarly states, "Different varieties of B. thuringiensis, which include, but need not be limited to, those listed in Table 3, have different host ranges . . . ; this probably reflects the toxicity of a given crystal protein in a particular host" (Adang '86, p. 2, first para.). Moreover, Adang teaches (Adang '86, pp. 30-31, bridging para.):

> Differences in rates of expression or developmental control may be observed when a given insecticide structural gene is inserted under control of different plant expressible promoters. Different properties, including but not limited to such properties as stability, intercellular or intracellular localization or excretion, solubility, target specificity, and other functional properties of the expressed protein itself may be observed in the case of fusion proteins depending upon the insertion site, the length and properties of the segment of T-DNA protein included within the fusion protein and mutual interactions between the components of the fusion protein that effect folded configuration thereof, all of which present numerous opportunities to manipulate and control the functional properties of the insecticidal protein product, depending upon the desired physiological properties within the plant cell, plant tissue, and whole plant.

Consistent with our understanding that "amounts insecticidal to Lepidopteran insects" means those amounts which destroy or control Lepidopteran insects, Adang suggests:

> One object of this invention is to confer pest resistance, specifically insect resistance, to a plant. . . . Another object is to provide novel specialized insecticidal tissues for a plant, in particular a means for producing on a normal dicot a gall which contains within its tissue an insecticidal protein.

(Adang '86, p. 20, first paragraph under SUMMARY OF THE INVENTION); and

> The introduction and expression of the structural gene for an insecticidal protein can be used to protect a crop from infestation with insect larvae . . . Pests which may be controlled by means of the present invention and the crops that may be protected from them include, but are not limited to, those listed in Tables 1 and 2. . . . A plant containing in its tissues insecticidal protein will control this recalcitrant type of insect . . . . [S]mall larvae are most sensitive to insecticidal protein and the protein is always present, minimizing crop damage . . . .

(Adang '86, pp. 22-23, bridging para.).

Adang explains (Adang '86, p. 27, first full para., p. 28; emphasis added):

> Insecticidal protein: As used herein includes a bacterial protein toxic in any way to insects. This includes a protein or peptide that is directly or indirectly toxic or growth inhibitory under any circumstances . . . . This also includes proteins that are upon contact, ingestion, or respiration, where alone or in combination with other material, at any time within the life cycle of an insect, including egg, larva, pupa, nymph, and adult

> stages. . . . The term crystal protein should be understood to refer to both the protoxin and toxin forms . . . .

Adang adds that "[d]ifferences in rates of expression may be observed when a given gene is inserted at different locations within T-DNA . . ." (Adang '86, p. 27, first full para.; emphasis added). Nevertheless, Adang teaches that "the toxic properties of expressed insecticidal protein can be used to identify transformed tissue" (Adang '86, p. 33). In an example, Adang reports (Adang '86, p. 38, first full para.; emphasis added):

> Insect larvae fed extracts of strains harboring p123/58-3 or p123/58-10 did not grow and all larvae died in 2 to 5 days. There was no apparent difference between the larvae fed these extracts and those fed insecticidal protein purified from cells of B. thuringiensis.

According to Adang, regenerated plants and "their insecticidal protein-containing descendants are resistant to infestation by larve [sic] of insects . . . by virtue of the toxic effect such larvae experience when eating from such plants" (Adang '86, pp. 44 and 49). Adang ultimately reports success in terms of the ratio of dead larvae (% Mortality) to total larvae allowed to consume tomato plant tissue showing insecticidal activity in bioassays relative to the ratio of dead larvae (% Mortality) to total larvae allowed to consume control tomato plant tissue (Adang '86, pp. 73-75).

Therefore, we conclude, consistent with the specifications and examples of both Adang and Fischhoff, that tomato plants encompassed by Count 1 (1) must have been regenerated from a tomato plant cell transformed by a full length Bt crystal protein gene which encodes Bt crystal protein of about 130 kD under control of a promoter which directs expression of said structural gene in said tomato plant cell, and (2) must produce amounts of Bt crystal protein protoxin of about 130 kD which destroy or control Lepidopteran insects in any way.

4. Decisions on motions

A. Fischhoff's preliminary motions

Fischhoff's Motion No. 1

Fischhoff moves (Paper No. 35) under 37 CFR § 1.633(c)(3) to designate Adang's Claims 15, 24, 42, and 44 as corresponding to Count 1. In a decision on motions entered April 30, 1996, an Administrative Patent Judge (APJ) denied Fischhoff's motion (Paper No. 121, p. 6-7). Upon further consideration, we hereby GRANT Fischhoff's motion.

Adang's Claims 15, 24, 42, and 44 are all broadly directed to (1) methods of "controlling insects harmful to plants" (Claims 15 and 44), most comprehensively comprising transforming plant

cells using a Bt crystal protein gene which encodes a Bt crystal protein under control of a promoter effective to promote expression of said gene in plant tissue cells regenerated from said transformed plant cells, regenerating insecticidal "plant tissue" (Claim 15) from the transformed plant cells, and allowing insects to feed on the "plant tissue" (Claims 15 and 44), and (2) insect-resistant "plant tissue" (Claims 24 and 42) prepared by said methods (Paper No. 35, pp. 2-4). Even though Claims 15, 24, 42, and 44 are directed to subject matter which is both broader and narrower in scope than the scope of subject matter encompassed by claims which have been designated as corresponding to Count 1, the patentability of the subject matter defined by Claims 15, 24, 42, and 44 stands rejected by an examiner as unpatentable for a variety of reasons (Adang '91, Papers No. 26 and No. 27). Nevertheless, we hold that the rejected claims define the "same patentable invention" as Count 1 of this interference and should therefore be designated as corresponding to the count.[3]

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[3] 37 CFR § 1,637(c)(3) reads (emphasis added):

> A preliminary motion seeking to designate an application or patent claim to correspond to a count shall:

(continued...)

Claims 16, 17, 22, 25-27, 29-32, 34, 40, 43, 46-50, and 57 of Adang '91, all of which have been designated as corresponding to the count, are directed to (1) regenerated transformed plants generally (Claims 25, 43, 47, and 48) or tomato plants specifically (Claim 57), and (2) regenerable transformed plant cells or tomato plant cells (Claims 16, 17, 22, 26, 27, 29-32, 34, 40, 46, 49, and 50). Adang's specification teaches that the claimed plants are regenerated from the transformed plant cells and used, all by means and methods acknowledged to be known in the art (Adang '91, p. 37, l. 3, to p. 38, l. 12). We hold that the regenerated tomato plant tissue Adang claims, the regenerated tomato plant cells Adang claims (Fischhoff does not dispute the designation of Adang's tomato cell claims as corresponding to the count), and known methods of making and using the same, would

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[3](...continued)

(I) Identify the claim and the count.

(ii) Show the claim <u>defines the same patentable invention</u> as another claim whose designation as corresponding to the count the moving party does not dispute.

37 CFR § 1.601(n) reads:

> Invention "A" is the *same patentable invention* as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". . . . .

have been obvious to persons having ordinary skill in the art in view of the regenerated tomato plants Adang claims which are designated as corresponding to the count. Because Fischhoff does not dispute that Adang's regenerated tomato plant cell claims define the same patentable invention as Adang's regenerated tomato plant claims, we hold that Adang's claimed regenerated tomato plant tissue (the tissue being a composite of the cells), and methods of making and using the same, also would have been obvious over, and define the same patentable invention as, Adang's claimed regenerated tomato plants. The APJ's presumption (Paper No. 121, pp. 6-7) that all the subject matter encompassed by a claim corresponding to Count 1 must be patentable is inconsistent with the subject matter encompassed by claims which already have been designated as corresponding to Count 1 (Interference 103,324, Paper No. 2). See also Orikasa v. Oonishi, 10 USPQ2d 1996, 2002 n.19 (Comm'r 1989)(emphasis added):

> An examiner may designate a rejected claim as corresponding to a count provided: (1) the claim covers both patentable and unpatentable subject matter; (2) the patentable subject matter of the claim is to the same patentable invention as the count; and (3) the unpatentable subject matter of the claim is not the same patentable invention as the count.

In accordance with 37 CFR § 1.637(c)(3), Fischhoff's preliminary motion under 37 CFR § 1.633(c)(3) seeking to

designate Claims 15, 24, 42, and 44 as corresponding to the count identifies both the claims and the count and "[s]how[s that] the claim[s] define[] the same patentable invention as another claim whose designation as corresponding to the count the moving party does not dispute" (emphasis added). In our view, Adang's Claims 15, 24, 42, and 44 "define the same patentable invention" as one or more of Claims 16, 22, 25-27, 29-32, 34, 46-50, 57, 40, and 43. Fischhoff's motion is GRANTED.

Accordingly it is ORDERED that

Claims 15, 16, 22, 24-27, 29-32, 34, 40, 42-44, 46, 47-50, and 57 of Adang '91 are designated as corresponding to Count 1 of this interference.

Fischhoff Motion No. 2

Fischhoff moves (Paper No. 36) under 37 CFR § 1.633(a) for judgment that Claims 16, 22, 25-27, 29-32, 40, 43, 46, and 47-50 of Adang '91 (a file-wrapper continuation of Adang '88), are unpatentable under 35 U.S.C. § 112, first paragraph. In a decision on motions entered April 30, 1996, an APJ deferred Fischhoff's motion (Paper No. 121, p. 7). While Adang '91 is a continuation of Adang '88, which itself is a continuation-in-part of Adang '86 (itself a continuation-in-part of Adang '83), only the specification of Adang's involved Adang '91 must provide a

"written description of the invention, and the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art . . . to make and use the same . . ." to satisfy the first paragraph of 35 U.S.C. § 112. "[E]arlier specifications are relevant only when benefit of an earlier filing date is sought under 35 U.S.C. § 120." Reiffin v. Microsoft Corp., ___ F.3d ____, ____, 54 USPQ2d 1915, 1918 (Fed. Cir. 2000).

In the BRIEF OF THE PARTY FISCHHOFF ET AL. ON FINAL HEARING (FB) (Paper No. 215), Fischhoff did not raise the issue of the patentability of Claims 16, 22, 25-27, 29-32, 40, 43, 46, and 47-50 with respect to Adang's involved Application 07/713,624 (Adang '91) under 35 U.S.C. § 112, first paragraph. Rather, Fischhoff argues that Adang's grandparent Application 06/848,733, filed April 4, 1986 (Adang '86), and Adang's great grandparent Application 06/535,354, filed September 26, 1983 (Adang '83), do not provide an adequate written description of the subject matter claimed and would not have enabled one skilled in the art to make and use the subject matter presently claimed. With respect to the patentability of claims in Adang's involved application under 35 U.S.C. § 112, first paragraph, the presence or absence of a

written description and enabling disclosure in the parent applications is totally irrelevant. Reiffin v. Microsoft Corp., ___ F.3d at ____, 54 USPQ2d at 1918. Fischhoff has not provided evidence or argument sufficient to satisfy its burden of proving that the claims in the involved application are not fully supported by the specification of Adang's involved application.[4] Fischhoff's PRELIMINARY MOTION FOR JUDGEMENT . . . UNDER 37 CFR § 1.633(a) THAT PARTY ADANG ET AL.'S CLAIMS . . . ARE UNPATENTABLE UNDER 35 U.S.C. § 112 (Paper No. 2), asserting that Adang's Claims 16, 22, 25-27, 29-32, 40, 43, 46 and 47-50 are unpatentable under 35 U.S.C. § 112, first paragraph, is DENIED.

Fischhoff Motion No. 3

Fischhoff moves (Paper No. 37) under 37 CFR § 1.633(a) for judgment that Claims 15, 24, 42, and 44 of Adang '91 (a file-

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[4] The burden of proof rests with the moving party. 37 CFR § 1.637(a). We note Fischhoff's statement on page 10 of the principal brief that Adang has the burden of proving the patentability of claims corresponding to the count which have been indicated on Form 850 by the examiner to be unpatentable. No action need be taken by Adang with respect to the unpatentability of such claims unless unpatentability is raised by a timely preliminary motion under 37 CFR § 1.633(a). The burden of proof for the preliminary motion would be on the moving party even if the grounds of unpatentability raised by the preliminary motion were the same as those raised by the examiner. "Unpatentable" claims which survive the interference will be subject to further prosecution when the application returns to ex parte examination.

wrapper continuation of Adang '88), are unpatentable under 35 U.S.C. § 112, first paragraph (Paper No. 37). In a decision on motions entered April 30, 1996, an APJ dismissed Fischhoff's motion because Fischhoff's motion 1 to designate Claims 15, 24, 42, and 44 as corresponding to Count 1 was denied (Paper No. 121, p. 7). The motion is being reviewed at Final Hearing because Fischhoff's motion 1 has now been granted. The theory of unpatentability is the same as that raised in Fischhoff's motion 2 (Paper No. 36). For reasons stated above with respect to Fischhoff's motion 2 under 37 CFR § 1.633(a) for judgment that Claims 16, 22, 25-27, 29-32, 40, 43, 46, and 47-50 of involved Adang '91 (a file-wrapper continuation of Adang '88), are unpatentable under 35 U.S.C. § 112, first paragraph, this motion also is DENIED.

Fischhoff Motion No. 11

Fischhoff moves under 37 CFR § 1.633(g) to attack the benefit of the April 4, 1986, filing date of continuation-in-part Adang '86 accorded Adang for Count 1 (Paper No. 23). In order to be accorded benefit of the filing date of an earlier filed application, the original specification of the earlier filed application must satisfy the requirements of 35 U.S.C. § 112, first paragraph, for one embodiment of the count, not the full

scope of the invention defined by the count or the claims corresponding to the count. Hunt v. Treppschuh, 523 F.2d 1386, 1389, 187 USPQ 426, 429 (CCPA 1975); Weil v. Fritz, 572 F.2d 856, 865-866 n.16, 196 USPQ 600, 608 n.16 (CCPA 1978). The patentability under 35 U.S.C. § 112, first paragraph, of the full scope of the subject matter to which a party's broad claims designated as corresponding to the count are directed is immaterial. Thus, to support its motion under 37 CFR § 1.633(g) to attack the benefit of the April 4, 1986, filing date accorded party Adang (Paper No. 2), it is Fischhoff's burden to establish by a preponderance of the evidence that Adang '86 reasonably (1) would not have described an embodiment encompassed by Count 1 to a person skilled in the art at the time Adang '86 was filed on April 4, 1986, and at the same time, (2) would not have enabled a person skilled in the art to make and use that embodiment.

Fischhoff appears to argue both that Adang '86 does not provide the requisite written description of an embodiment defined by Count 1 and would not have enabled one skilled in the art to make and use that embodiment without undue experimentation. Whether Adang '86 provides an adequate written description under 35 U.S.C. § 112, first paragraph, of an embodiment encompassed by Count 1, is a question of fact.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Whether Adang '86 would have enabled persons skilled in the art to make and use an embodiment encompassed by Count 1 without undue experimentation, is a question of law. In re Vaeck, 947 F.2d at 495, 20 USPQ2d at 1444.

University of California v. Eli Lilly and Co., 119 F.3d 1559, 1566-67, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), instructs:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed Cir. 1989)("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, the applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA . . . "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required

is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

To satisfactorily describe an invention of Count 1, Adang '86 must adequately describe every aspect of one embodiment of the subject matter defined by Count 1. Accordingly, the specification of Adang '86 must adequately describe:

(a) a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects;

(b) a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects;

(c) tomato plant cells transformed by a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects under control of a promoter;

(d) production of Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects by transformed tomato plant cells;

(e) tomato plants regenerated from tomato plant cells transformed to produce Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects; and

(f) tomato plants which produce enough Bt crystal protein of about 130 kD to destroy or control Lepidopteran insects in any way.

Of record in this interference, we find declarations of many skilled artisans. Although we find that the level of skill in this art is high, we are not at all surprised that the views of Adang's declarants differ greatly from the views of Fischhoff's declarants with regard to subject matter described and enabled by Adang '86. We find that the knowledge and skill in the art was increasing in leaps and bounds at the time Adang '86 was filed (April 4, 1986). As evidence, see the number of background publications cited at pages 1-20 of the Adang '86 specification and their publication dates. Considering the state of the art at the time Adang '86 was filed, Fischhoff moves for a finding that Adang '86 does not describe an embodiment of Count 1 and a conclusion that Adang '86 would not have enabled one skilled in the art to make and use an embodiment of Count 1 in the manner required by the first paragraph of 35 U.S.C. § 112. Given the incipient state of the art and the air of uncertainty associated therewith at the time Adang '86 was filed, we find that all of the contradictory views of the parties' declarants, all persons skilled in the art, with regard to the level of knowledge and

skill persons having ordinary skill in the art would have had and all that they would have learned from and/or reasonably expected in view of the disclosure of Adang '86 at the time it was filed, must be weighed carefully. Having considered all the declaratory evidence proffered by Adang and Fischhoff, the complete disclosures of Adang '88, Adang '86, Adang '83, and Fischhoff '86, and all the published information of the inventors themselves and others of record, we find the views expressed and evidence presented by Adang's declarants more convincing on the written description issue and the views expressed and evidence presented by Fischhoff's declarants more convincing on the enablement issue.

We find that Adang '86 describes a Bt crystal protein of about 130 kD which is toxic to lepidopteran insects. Adang '86 teaches (Adang '86, p. 1):

> Bacillus thuringiensis . . . forms a proteinaceous crystalline inclusion during sporulation. . . . The crystal protein, often referred to as the w-endotoxin, has two forms: a nontoxic protoxin of approximate molecular weight (MW) of 130 kilodaltons (kD), and a toxin having an approx. MW of 67 kD.

Adang '86 also teaches (Adang '86, p. 2, first para.):

> B. thuringiensis and its crystalline endotoxin are useful because the crystal protein is an insecticidal protein known to be poisonous to the larvae of over a hundred of species of insects, most commonly those of the orders Lepidoptera and Diptera.

The 130 kD protoxin and its properties appear to have been well known in the art long before April 4, 1986 (Adang '86, p. 1, citing a 1983 article by Klowden).

Next, we search Adang '86 for a written description of a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects. As indicated in Fiers v. Revel, 984 F.2d at 1171, 25 USPQ2d at 1606, structural DNA which encodes the protein may be adequately described by its structure, formula, chemical name, or properties. However, structural DNA cannot be adequately described by a mere wish or plan for obtaining it. Id. The description requirement of 35 U.S.C. § 112, first paragraph, is satisfied "by describing the invention, with all its claimed limitations, not that which makes it obvious." Lockwood v. American Airlines, Inc., 107 F.3d at 1572, 41 USPQ2d at 1966.

Adang '86 describes a full length Bt crystal protein gene which encodes a Bt crystal protoxin of about 130 kD which is toxic to Lepidopteran insects as follows (Adang '86, pp. 2-4; citations omitted):

> The crystal protein gene usually can be found on one of several large plasmids that have been found in Bacillus thuringiensis . . . . Whiteley's group . . . reported the cloning of the toxin from B. thuringiensis var. kurstaki strains HD-1-Dipel and HD-73 . . . . Crystal protein from the HD-1-Dipel gene which was toxic

> to larvae, immunologically identifiable, and the same size as authentic protoxin, was observed to be produced by transformed E. coli cells containing pBR322 clones or subclones. . . . Klier A et al. . . . have reported the cloning of the crystal protein gene from B. thuringiensis strain berliner 1715 in pBR322. Using the enzyme BamHI, a large 14 kbp fragment carrying the crystal protein gene was moved into the vector pHV33, which can replicate in both E. coli and Bacillus. In both E. coli and sporulating B. subtilis, the pHV33-based clone directed the synthesis of full-size (130 kD) protoxin which formed cytoplasmic inclusion bodies and reacted with antibodies prepared against authentic protoxin. Extracts of E. coli cells harboring the pBR322 or pHV33-based plasmids were toxic to larvae. . . . Chang S (1983) . . . reported that the DNA sequence of a complete HD-1 gene had been publicly presented . . . and that the HD-1 toxin moiety resides in the amino-terminal 67 kD peptide.

It appears from the above that Adang '86 provides a written description of a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects. Citing an article by Kronstad, Adang '86 teaches that a full length Bt crystal protein gene has been located on a large plasmid found in Bt (Adang '86, p. 2). Citing the Whiteley, Klier, and Held groups, Adang '86 teaches that the a full length Bt crystal protein gene has been cloned from Bt var. kurstaki strains HD-1-Dipel and HD-3 and a Bt berliner 1715 strain, successfully inserted into E. coli and/or Bacillus plasmid vectors, and expressed therein with reported production of a protein insecticidal to larvae which was identified as a 130 kD Bt protoxin (Adang '86, pp. 2-4). Thus, Adang '86 appears

to have provided an objective written description of a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects. Accordingly, Adang '86 appears to describe a gene defined by Count 1 in the manner required by 35 U.S.C. § 112, first paragraph.

Example 11 of Adang '86 (Adang '86, pp. 61-75) purportedly "teaches isolation of a clone having the 3'-end of the insecticide gene carried by p123/58-10, and the reconstruction of a full-length HD-73 crystal protein gene" (Adang '86, p. 61, first full para.); i.e., "[t]o reconstruct a complete protoxin gene" (Adang '86, p. 61, second full para.; emphasis added); e.g., (Adang '86, p. 62, lines 9-12):

> A transformant was identified that harbored a plasmid, designated pBt73-16, carrying a complete protoxin gene. E. coli HB101 (pBT73-16) is on deposit at the Northern Regional Research Center, 1815 N. University St., Peoria, Illinois 61604 USA, as NRRL B-15759.

Adang also points to the part of Adang '86 which states (Adang '86, p. 4):

> Chang S (1983) Trends Biotechnol. 1:100-101, reported that the DNA sequence of a complete HD-1 gene had been publicly presented (ref. 5 therein), and that the HD-1 toxin moiety resides in the amino-terminal 67 kD peptide.

However, Fischhoff denies the truth of the statement, supports its denial with evidence, and further denies that the sequence of a full length Bt crystal protein gene encoding a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects is described in any of Adang '83, Adang '86, Chang (1983), or reference 5 cited in Chang (1983)(Reply Brief of the Party Fischhoff (FRB)(Paper No. 228), pp. 4-5). We find the parties' debate whether or not the complete sequence of a full length Bt crystal protein gene which encodes Bt crystal protein of about 130 kD was fully disclosed in 1983 immaterial to the issues placed before us.[5]

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[5] On considering the count as a whole, we conclude that the full length Bt crystal protein gene and the promoter which controls its expression in the transformed tomato cells used to regenerate the new transgenic tomato plants of Count 1, are defined in a manner sufficient to allow persons having ordinary skill in the art to identify, compare, and distinguish regenerated tomato plants encompassed by the count from tomato plants previously described and/or claimed by others. Even though the full length Bt crystal protein-encoding gene and promoter control sequences are not defined by their chemical structure, i.e., their respective nucleic acid sequences, they may be and are adequately defined in Count 1 by the properties of the protein encoded, the amount of protein production directed, the source of the sequences, deposits comprising the sequences, vectors which comprise the sequences, and the manner in which the vectors were constructed, isolated, utilized, etc. See Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991)("A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to

(continued...)

Adang '86 describes a vector comprising a full length Bt crystal protein gene encoding a Bt crystal protein of about 130 kD which is insecticidal to Lepidopteran insects. We find that a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is insecticidal to Lepidopteran insects is identified, available, and useful as part of a vector and is, therefore, described in compliance with the first paragraph of 35 U.S.C. § 112.

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[5](...continued)
obtain it.") Moreover, here the count is not directed to a DNA construct but to tomato plants regenerated from tomato plant cells transformed by a DNA construct to produce specific amounts of a Bt crystal protein with recognizable properties. We are reminded of the instruction of In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963) (emphasis added):

> From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. The graphic formulae, the chemical nomenclature, the systems of classification and study such as the concepts of homology, isomerism, etc., are mere symbols by which compounds can be identified, classified, and compared. But a formula is not a compound and while it may serve in a claim to identify what is being patented, as the metes and bounds of a deed identify a plot of land, the thing that is patented is not the formula but the compound identified by it. And the patentability of the thing does not depend on the similarity of its formula to that of another compound but of the similarity of the former compound to the latter. There is no basis in law for ignoring any property in making such a comparison.

Adang states, "[T]he structural requirements in this regard are best described in functional terms" (Adang Application 06/848,733, p. 30).

Next, we search Adang '86 for a written description of tomato plant cells transformed by a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects under control of a promoter, expression of the gene in the tomato plant cells, tomato plants regenerated from the transformed tomato cells, and regenerated tomato plant production of amounts of Bt protoxin insecticidal to Lepidopteran insects. The word "tomato" appears once in Adang '86 in its plural form. Adang '86 includes "tomatoes" in the Table 2 listing of "Plants recommended for protection by B. thuringiensis insecticidal protein" (Adang '86, p. 87). One mention of "tomatoes" is enough if one skilled in the art can conclude therefrom that Adang invented the subject matter claimed. University of California v. Eli Lilly and Co., 119 F.3d at 1566-67, 43 USPQ2d at 1404.

Fischhoff's arguments and expert opinions notwithstanding, we find that Adang '86 (1) describes transformed foreign plant cells using Bt crystal protein genes which encode known Bt crystal proteins which are toxic to Lepidopteran insects under control of a promoter, (2) provides an example (Adang '86, Example 12, pp. 62-75) said to show the successful transformation of cells of at least one of the 94 kinds of plants recommended

for protection by Bt insecticidal protein, namely tobacco, by a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects, and (3) describes at least 94 kinds of plants which may be protected by Bt insecticidal proteins, including tomatoes, each of whose plant cells are said to be capable of being transformed by Bt crystal protein genes which encode Bt crystal proteins which are toxic to Lepidopteran insects.

Adang '86 introduces Example 12 as follows (Adang '86, p. 62):

> This Example teaches the insertion of the full length Bacillus thuringiensis insecticide gene between a T-DNA gene promoter and a polyadenylation (poly(A) addition) signal, the transfer of the insecticide gene to tobacco via a sub-Ti plasmid, the regeneration of the plants containing the gene, and expression of this gene under control of the T-DNA promoter in plant cells.

But for the fact that Count 1 is directed to tomato plants, and our finding that Example 12 of Adang '86 specifically describes insecticidal tobacco, the above-quoted introduction to Example 12 appears to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, for an invention encompassed by Count 1.

That Adang '86 describes tomato plants regenerated from tomato plant cells transformed by a full length Bt crystal

protein gene encoding a Bt crystal protein of about 130 kD which is toxic to Lepidopteran insects under control of a promoter which directs production of the 130 kD protoxin in amounts effective to destroy or control Lepidopteran insects, in the manner required by the first paragraph of 35 U.S.C. § 112, and not merely a wish or plan for obtaining it (Fiers v. Revel, 984 F.2d at 1171, 25 USPQ2d at 1606), is evident. See the following additional description in Adang '86:

> The invention is exemplified in one of its embodiments by the insertion of the full length structural gene of Bacillus thuringiensis insect toxic protein into a sub-Ti plasmid so that the toxin gene is placed under the control of T-DNA plant active regulation sequences (ORF24). The sub-Ti plasmid containing the plant expressible crystal protein gene was introduced into tobacco cells. Tobacco plants regenerated from these transformed cells were found to express crystal protein at levels measurable by ELISA techniques but also the leaves of these plants were found to be toxic to insect larvae.

(Adang '86, p. 21, second full para.; emphasis added); and

> The invention in principle applies to any introduction of an insecticide structural gene into any plant species into which foreign DNA (in the preferred embodiment T-DNA) can be introduced and in which said DNA can remain stably replicated. In general these taxa presently include, but are not limited to, gymnosperms and dicotyledenous [sic] plants, such as sunflower (family Compositeae),

> tobacco (family Solanaceae),[6] alfalfa, soybeans and other legumes (family Leguminoseae), cotton (family Malvaceae), and most vegetables. Pests which may be controlled by means of the present invention and the crops that may be protected from them include, but are not limited to, those listed in Tables 1 and 2,[7] respectively.

(Adang '86, pp. 22-23, bridging [para.). In our view, Fischhoff has not adequately explained why the specification of Adang '86 does not satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, for an embodiment of Count 1 of this interference.

Enablement is an entirely different matter. The question presented is whether Adang '86 would have enabled persons skilled in the art to (1) transform tomato plant cells, using a full length Bt crystal protein gene which encodes a known Bt crystal protein of 130 kD which is toxic to Lepidopteran insects, to produce Bt crystal protein of 130 kD, (2) regenerate tomato plants from the transformed tomato cells, and (3) produce Bt crystal protein of 130 kD in the tomato plants in amounts effective to destroy or control Lepidopteran insects, all without

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[6] Stedman's Medical Dictionary, 24th Edition, Williams & Wilkins, Baltimore, MD (1982), provides the following definition at page 1300 (emphasis added): "Solanaceae . . . . A family of plants that includes the genus Solanum (nightshade) and some 84 other genera comprising 1800 species, including the tomato and potato plants."

[7] Table 2 expressly includes tomatoes.

undue experimentation. The parties focus on the transformation and production aspects of enablement.

We note first that Adang '86 describes how to make and use an invention encompassed by Count 1 in terms which correspond in scope to those used in Count 1. Therefore, Adang '86 must be taken as in compliance with the enablement requirement of the first paragraph of § 112 absent sufficient reasons to doubt the objective truth of the statements contained in Adang '86 which must be relied on for enabling support. In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971). As the moving party, Fischhoff must show that persons skilled in the art would not have been enabled by the Adang '86 disclosure to make and use a tomato plant of Count 1 in the manner required under 35 U.S.C. § 112, first paragraph.

The first paragraph of 35 U.S.C. § 112 requires that the specification provide sufficient information and/or guidance to enable persons skilled in the art to succeed without undue experimentation. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991):

> The first paragraph of 35 35 U.S.C. § 112 requires, inter alia, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and

> use the invention without "undue experimentation." In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (citing Ex parte Forman, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986)), instructs:

> Factors to be considered in determining whether a disclosure would require undue experimentation . . . include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The following evidence supports Fischhoff's motion.

(1) Adang argued that "Perlak's comparison[, (Perlak's Declaration I (FR, pp. 142-147) "describes experiments that were conducted in order to compare the inherent variability of three different bioassays for determining expression of *B.t.* crystal protein in plants and is meant to discredit Adang's Example 12" (AB, p. 46, first full para.),] . . . is invalid because Perlak used a completely different strain of tobacco from the strain Adang used in Adang's Example 12" (AB, p. 46, second full para.). The argument suggests that the skilled artisan's capacity to transform tobacco plant cells and regenerate tobacco plants toxic to Lepidopteran insects depends to a substantial degree on the

strain of tobacco. We do not agree with Fischhoff that "Adang effectively concedes, to the extent that it has shown any bioactivity as a result of the expression of a full-length B.t. gene in tobacco (which claim Fischhoff refutes), that Adang is limited to the particular variety of tobacco utilized by Adang" (FRB, pp. 10-11, bridging para.). Nevertheless, Adang's reply to Perlak's comparison (quoted above) indicates that persons skilled in the art would not have expected success in regenerating tomato plants insecticidal to Lepidopteran insects from dicotyledonous tomato plant cells transformed by a full length Bt crystal protein gene based on evidence that tobacco cells had been successfully transformed by the same genetic construct and one strain of dicotyledonous tobacco plants insecticidal to Lepidopteran insects had been regenerated therefrom.

(2) Vaeck et al. (DeGreve), European Patent Application 193,259, published September 3, 1986, teaches (DeGreve, p. 3, line 10, to p. 4, line 10; emphasis added):

> Although certain chimeric genes have now successfully been expressed in transformed plant cells, such expression is by no means straightforward. Various lines of evidence indicate that the level of expression of the foreign genes of non-plant origin not only varies greatly in different transformed tissues but are in general very low. Such low levels of gene expression could be due to several reasons: first, incomplete transcription of the gene resulting from inadvertent transcription termination signals; second, inefficient processing of the messenger RNA; third,

> impaired transport of the messenger RNA from the nucleus to the cytoplasm; fourth, instability of the cytoplasm messenger RNA; fifth, inefficient translation of the cytoplasm messenger RNA; and sixth, instability of the protein due to its susceptibility to plant specific proteins. Consequently, the successful transformation of plant cells using vectors . . . is not necessarily predictable prior to attempting a desired transformation.
>
> Engineering of differentiated plant cells and their progeny to express the Bt2 polypeptide and/or a truncated version thereof and/or polypeptide having substantial sequence homology thereto is far more difficult than other genes such as antibiotic resistance genes or other plant genes such as thaumatin due to one or more of the following: (1) the large size of the Bt2 toxin, even in its truncated form; (2) the particular properties of the Bt2 polypeptide (such as, but not limited to, solubility of the polypeptide); (3) the potential toxicity of the Bt2 polypeptide toward the plant cells; or (4) the Bt2 polypeptide synthesized in the plant cells and their progeny must retain substantially the same properties as the crystal protein synthesized in bacteria.

DeGreve generally teaches that "introduction and integration of one or more chimeric genes coding for polypeptide toxins produced by [Bt] . . . is achieved by" (DeGreve, pp. 23-25):

> (1) isolation of at least one DNA fragment from . . . [Bt] coding for a polypeptide toxin by digestion of bacterial DNA and inserting the mixture of DNA fragments obtained into a cloning vehicle harbored in a bacterial host; and
>
> (2) identification of bacterial clones harboring DNA fragments coding for said polypeptide toxin; and
>
> (3) characterization of the structure of the DNA fragment coding for said polypeptide toxin; and

(4) removal of unwanted DNA sequences flanking the desired DNA fragment; or

(5) synthesis of a DNA fragment having substantial sequence homology and exhibiting a similar structure to a DNA fragment coding for Bt2; or

(6) construction of a DNA fragment containing the DNA fragment from (4) fused to a DNA fragment encoding an identification polypeptide to produce a fusion polypeptide; and

(7) insertion of said DNA fragment from (4) or (5) or (6) into plasmid vectors under control of plant regulator sequences harbored in a bacterial host; and

(8) introduction of plasmids from (7) by conjugation (or mobilization) in a bacterial host harboring suitable helper plasmids; and

(9) conjugation of bacterial clones from (8) to Agrobacterium tumefaciens harboring an acceptor Ti plasmid vector; and

(10) identification of Agrobacterium tumefaciens which contain the desired chimeric gene; and

(11) contacting plant cells with Agrobacterium tumefaciens from (10); and

(12) identification of transformed plant cells from appropriate culture media; and

(13) immunological detection of Bt2 antigens present in extracts from transformed plant cells; and

(14) propagating transformed plant cells to regenerate a differentiated plant.

DeGreve's outline above of the requisite procedural steps for introduction and integration of chimeric genes coding for polypeptide toxins produced by Bt into plants is followed by

better than 100 pages of engineering specifics, examples, and tabulated results (DeGreve, pp. 29-140). Nevertheless, DeGreve merely contemplates future success, particularly with dicotyledonous plants, most particularly with cotton, sugarbeet, soybean, rape, cabbage, lettuce, and beans (DeGreve, p. 27, lines 3-12; emphasis added):

> It is contemplated that plants, particularly dicotyledonous plants, other than those described below in the examples can be transformed such as cotton, sugarbeet, soybean, rape and vegetables such as cabbage, lettuce and beans. Transformed plant cells and their progeny are protected against certain insect pests by expressing an insect controlling amount of polypeptide toxin. By controlling amount is meant a toxic (lethal) or combative (sublethal) amount of polypeptide toxin.

(3) Adang et al., "Characterized full-length and truncated plasmid clones of the crystal protein of Bacillus thuringiensis subsp. kurstaki HD-73 and their toxicity to Manduca sexta," Gene, Vol. 36, pp. 289-300 (1985)(Adang Gene), teach (Adang Gene, pp. 289-290):

> . . . B. thuringiensis produces a proteinaceous crystal that is lethal to most lepidopteran . . . larvae . . . The crystal protein is a polypeptide of approx. 130 kDal. Crystals which are ingested by susceptible larvae are solubilized and the 130-kDal protoxin is degraded to a biologically active polypeptide of 68 kDal . . .
>
> . . .
>
> In this study we describe the molecular cloning of the crystal protein gene from B. thuringiensis subsp.

> kurstaki HD73 into E. coli. This E. coli recombinant synthesizes a polypeptide of 133 kDal, and cell extracts are toxic to larvae of the tobacco hornworm, Manduca sexta (L.). The complete nucleotide sequence of the gene was determined, and the transitional start site and the deduced amino acid sequence are presented. . . . E. coli harboring these truncated genes demonstrate that the N-terminal 68-kDal polypeptide is toxic, but at a greatly reduced level, when assayed against M. sexta larvae.

Adang Gene presents the following description (Adang Gene, p. 293, col. 1, second full para.):

> The complete nt sequence of the crystal protein gene from strain HD-73 is shown in Fig. 3, beginning with an ATG initiation codon at position 388 and ending with a TAG termination codon at position 3924. The total length of the HD-73 gene is 3537 nt, coding for 1178 aa and encoding a protein of M_r 133 330.

Adang Gene reports (Adang Gene, pp. 297-98, bridging para.; emphasis added):

> Table II lists the relative toxicities of cell extracts containing full-length or truncated crystal protein genes against M. sexta larvae. As expected E. coli [pBT 73-16] which expresses the complete protein is most toxic to the larvae and is used for subsequent comparisons with the truncated clones. However, E. coli [pBT73-10] and E. coli [pBT73-3Ava] containing truncated genes are both lethal to the larvae but only 7.6% as toxic as the full length peptide. These results indicate that the N-terminal 68-kDal peptide is sufficient for minimal biological activity. The 106-kDal peptide of E. coli [pBT73-10] is not any more toxic than the 68-kDal product of clone E. coli [pBT73-3Ava].

Most pertinent to the legal issues presented by this interference is the following statement from the discussion in

Adang Gene (Adang Gene, p. 298, col. 2, second full para.; emphasis added):

> E. coli pBT73-16 contains a complete crystal protein gene, yet peptides were observed ranging from the expected 133 kDal to 68 kDal. One explanation for this range in peptide sizes is that the translation product is not stable in E. coli but is proteolytically cleaved to a relatively stable 68-kDal peptide. An alternative explanation is that premature termination of transcription or translation could be occurring. . . .

This last portion of the Adang Gene discussion is material to the issues presented in this interference essentially for three reasons. First, it shows that one skilled in the art reasonably could not have predicted whether any select promoter sequence would direct expression of a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD in a foreign host cell transformed by said full length Bt crystal protein gene and production of a Bt crystal protein of about 130 kD by said foreign host cell. Second, it shows that in 1985 one skilled in the art reasonably could not have predicted whether any select promoter sequence would direct expression of a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD in a foreign host cell transformed by said full length Bt crystal protein gene and production of Bt crystal protein of about 130 kD in amounts capable of destroying or controlling Lepidopteran insects. Third, it shows that evidence that a

foreign host cell transformed by a Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD, produces a Bt crystal protein which is toxic to Lepidopteran insects does not establish that the foreign host cell has produced insecticidal amounts of a Bt crystal protein of about 130 kD.

(4) Vaeck et al. (Vaeck), "Transgenic plants protected from insect attack," Nature, Vol. 328, pp. 33-37 (1987), teach (Vaeck, p. 33, col. 1, first para.; emphasis added):

> The insecticidal activity [of toxins produced by Bt] resides in crystalline inclusion bodies produced during sporulation of the bacteria, which are composed of proteins (termed delta endotoxins) specifically toxic against a variety of insects. Different strains of B. thuringiensis differ in their spectra of insecticidal activity . . . The crystals dissolve in the alkaline conditions of the insect midgut and release proteins of relative molecular mass 65,000-160,000 (M_r 65K-160K) . . . which are proteolytically processed by midgut proteases to yield smaller toxic fragments.

Vaeck's 1987 publication cites their 1986 work for the following information (citations to ref. 9 and Fig. 1a omitted):

> We have reported the cloning of the bt2 gene from B. thuringiensis strain berliner 1715 and the characterization of the recombinant polypeptide expressed in Escherichia coli. This protein, termed Bt2, is 1,155 amino acids long and is a potent toxin to several lepidopteran larvae, such as those of Manducta sexta, a pest of tobacco. Bt2 is a protoxin and generates a smaller polypeptide of M_r 60K which retains full toxic activity. . . .
>
> In plant transformation experiments, we used chimeric genes containing the entire coding sequence of bt2 as well

> as the truncated genes. . . . Plasmid pLB884 contains the truncated . . . gene bt884 and encodes an NH_2-terminal fragment of Bt2 up to amino-acid position 610. In E. coli it produces a polypeptide of the expected size which is fully toxic towards insect larvae.

Most interesting above is Vaeck's reference to the 1986 report that E. coli transformed by a truncated bt2 gene "produces a polypeptide of the expected size which is fully toxic towards insect larvae". Id. More specific to experimentation with transgenic tobacco plants, Vaeck surprisingly reports (Vaeck, p. 35, cols. 1-2, bridging para.; emphasis added):

> Clear insecticidal activity was also detected in most of the 15 plants expressing the truncated bt884 gene, of which two-thirds induced more than 75% larval death. None of the plants transformed with the full length bt2 gene produced insect killing activity above levels obtained in NPTII-expressing control plants. These experiments indicate that for the promoter gene constructs we used, only truncated bt2 genes give rise to expression levels that are strongly insecticidal in transgenic tobacco.

Vaeck's work with transgenic tobacco plants emphasizes how very critical the choice of the control promoter is to production of the full length bt2 crystal protein gene in amounts insecticidal to Lepidopteran insects. Vaeck reports (Vaeck, pp. 35-36, bridging para.):

> Plants transformed with the truncated bt2 gene . . . contain approximately ten times more Bacillus protein than those transformed with the complete bt2 sequence (Table 2). Thus, the failure to obtain insect-resistant plants using the intact bt2 gene is most probably due to inefficient protein synthesis in these transformed plants.

That the art of expressing a full length Bt crystal protein gene which encodes Bt crystal protein under control of any select promoter in tobacco cells, not to mention tomato cells, in amounts insecticidal to Lepidopteran insects was highly unpredictable even in 1987 is evident from Vaeck's discussion (Vaeck, pp. 36-37; emphasis added):

> Four chimeric genes containing modified Bacillus toxin genes under control of the 2' promoter of the Agrobacterium TR DNA, have been transferred into tobacco plants. All contain the toxic core of the Bt2 protein; bt2 encodes the complete M_r 130K protoxin, bt884 is a 5' fragment of bt2 up to codon 610, Bt:neo23 and bt:neo860 encode fusion proteins which are relatively stable, both in bacteria and plants, and which retain full insect toxicity and NPTII activity.
>
> Insecticidal levels of toxin were produced when truncated Bacillus genes or fusion constructs were expressed in transgenic plants. . . .
>
> No significant insecticidal activity could be obtained using intact bt2 coding sequence, despite the fact that the same promoter was used to direct its expression. Intact Bt2 protein and RNA amounts in the transgenic plant leaves were 10-50 times lower than those for the truncated B. thuringiensis polypeptide or the fusion proteins. . . . Why the complete bt2 gene is not expressed at an equally high level in plant cells, is not known. Several parameters, such as differential RNA stability and translation efficiency might be important.
>
> . . .
>
> Our experiments illustrate the feasibility of engineering plants that defend themselves against lepidopteran insects which are sensitive to the

> B. thuringiensis berliner insect toxin. . . . To protect plants fully against these insects, higher levels of expression will be required. This might be achieved using chimeric Bacillus genes containing stronger plant-specific promoters. The 35S promoter of cauliflower mosaic virus . . . for example directs a 10-50-fold higher expression than the regular T-DNA promoters in plants. Alternatively, it may be possible to construct chimeric toxin genes with higher specific activity against important target insects. Transfer of different chimeric genes into a variety of crops may provide a new and environmentally safer method of controlling destructive insect pests.

We find that Vaeck's report of the state of the art in 1987 is an invitation to experiment rather than a report of success. Vaeck's experiments "illustrate the feasibility of engineering plants that defend themselves against lepidopteran insects which are sensitive to the B. thuringiensis berliner insect toxin" (Vaeck, p. 37, col. 1, first sentence). More importantly, we find that Vaeck's view of the state of the art in 1987 is far more substantiated and credible than is the view Adang's Brief for Final Hearing presents of the state of the art prior to 1987, i.e., on April 4, 1986, filing date of Adang '86.

(5) Barton et al. (Barton), "Bacillus thuringiensis δ-Endotoxin Expressed in Transgenic Vicotiana tabacum Provides Resistance to Lepidopteran Insects," Plant Physiol., Vol. 85, pp. 1103-09 (1987), teach (Barton, p. 1103, cols. 1-2, bridging para.; emphasis added):

> This report presents data on the development of transgenic tobacco plants that produce sufficient levels of B.t. toxin to either kill Lepidopteran insects or inhibit their feeding. Analysis of the expression of the chimeric gene in the resistant plants has revealed several problems which affect the levels of toxin gene expression. These problems must now be resolved in order to obtain additional insect resistant agricultural crops.

Barton notices yet other problems which must be resolved when determining whether plants regenerated from transformed plant cells produce sufficient levels of Bt toxin to destroy or control Lepidopteran insects. First, Barton teaches (Barton, p. 1104, col. 2, second full para.):

> Mature tobacco plants contain higher levels of secondary metabolites than freshly regenerated plants, so larvae with feed exposure to older plants were considerably less sensitive to B.t. toxin than neonatal larvae.

Next, Barton reports (Barton, p. 1105, col. 2, first full para.; emphasis added):

> Because the intact protoxin had seen extensive field use in microbial formulations, we initially attempted to express the entire 1176 amino acid toxin in plant cells. Our initial constructions were similar to those detailed here, but contained the entire toxin coding sequence. Following transformation and selections for kanamycin resistant transformants, we obtained tobacco calli that were shown by immunoblots to contain significant levels of intact protoxin (10-50 ng/mg protein). However, all such calli soon became necrotic and died. Any plants we were able to regenerate from our initial experiments were shown by hybridization analysis and immunoblots to contain either broken or inactive toxin genes . . . We eventually

> concluded that expression of intact δ-endotoxin was lethal to plant cells. In subsequent experiments, including those described in this report, we eliminated the protoxin carboxy terminus and found no evidence that the truncated toxin is deleterious to plant cell viability.

Use of the truncated gene did not solve Barton's problems (Barton, p. 1108-109, bridging para.):

> Our results and those presented elsewhere . . . indicate that the B.t. toxin presents unusual problems that must be overcome to obtain useful levels of toxin protein in plants. Our initial experiments led to the conclusion that expression of intact protoxin was in some way toxic to plant tissues, since transformants that contained . . . [the] toxin did not show the same apparent toxicity toward plant cells, the level of toxin mRNA obtained in our insect-resistant transformants remained quite low relative to the adjacent NPT-II gene, and relative to other chimeric genes. The low level of toxin-related RNA correlates with low levels of toxin protein. However, due to the high potency of the B.t. toxin toward susceptible insects, some transformants were resistant to M. sexta even when toxin protein was below detectable levels.

Finally, Barton indicates that his unique efforts to obtain useful levels of expression in tobacco are undergoing further analysis. "No accurate comparisons to alternative constructions are yet possible, since expression of chimeras prior to these modifications was too low to be detected" (Barton, p. 1109, first full para.). "To compound the problem of low levels of B.t. toxin-related RNA the use of slot blots to quantitate toxin-specific mRNA was found to be deceptive" (Barton, p. 1109, second full para.). The evidence "suggests that the toxin transcript is

unstable, possibly due to inefficient posttranscriptional processing or rapid turnover. We are exploring each of these possibilities . . ." (Barton, p. 1109, second full para.). Barton concludes (Barton, p. 1109, final para.; emphasis added):

> A detailed analysis of the present toxin gene expression, coupled with systematic alterations in primary and secondary characteristics of the transcript, will provide insight into problems specific to the expression of toxin protein in plants, as well as more generally to the expression of additional chimeras. Information resulting from such analysis is currently being applied to obtain cotton . . . resistant to Lepidopteran insects.

Collectively, Adang's tobacco species distinctions and the aforementioned publications raise substantial doubts that Adang '86 would have enabled persons skilled in the art as of its April 4, 1986, filing date, to regenerate a tomato plant which produces 130 kD Bt crystal protein in amounts effective to destroy or control Lepidopteran insects from a tomato plant cell transformed using a full length Bt crystal protein gene. The evidence shows that in 1986 the factors and problems associated with transformation of tobacco plant cells to express a full length Bt crystal protein gene encoding Bt crystal protein of about 130 kD, and regenerate of tobacco plants therefrom which produce a Bt crystal protein protoxin of about 130 kD in amounts which destroy or control Lepidopteran insects, were so numerous and misunderstood, and success in transforming tobacco plant

cells to express a full length Bt crystal protein gene encoding Bt crystal protein of about 130 kD, and regenerate tobacco plants therefrom which produce Bt crystal protein of about 130 kD in amounts which destroy or control Lepidopteran insects, was so rare and unpredictable, that persons skilled in the art having the disclosure of Adang '86 before them, even with one example of tobacco plant cell transformation, reasonably would not have expected to be able to successfully transform tomato plant cells by the same procedure to express a full length Bt crystal protein gene encoding Bt crystal protein of about 130 kD and regenerate tomato plants which produce Bt crystal protein of about 130 kD in amounts which destroy or control Lepidopteran insects therefrom, without undue experimentation. This is especially true where, as here, we find that Example 12 of Adang '86, does not establish that the transformed tobacco plants, which are therein described as having been regenerated from tobacco cells transformed by a full length Bt crystal protein gene encoding Bt crystal protein of about 130 kD and as having destroyed or controlled Lepidopteran insects, produced Bt crystal protein of about 130 kD in amounts effective to destroy or control Lepidopteran insects. Rather Example 12 merely identifies total Bt crystal protein without identifying the molecular weight of the Bt crystal

protein expressed. In other words, the example does not establish that the reported insecticidal activity was due to the expression of the 130 kD protein rather than expression of the toxic 67 kD protein.

Adang '86 teaches that "[a] transformant was identified that harbored a plasmid, designated pBt73-16, carrying a complete protoxin gene" (Adang '86, p. 62, last sentence before Example 12). However, Adang Gene taught in 1985 (Adang Gene, p. 298, col. 2, second full para.; emphasis added):

> E. coli pBT73-16 contains a complete crystal protein gene, yet peptides were observed ranging from the expected 133 kDal to 68 kDal. One explanation for this range in peptide sizes is that the translation product is not stable in E. coli but is proteolytically cleaved to a relatively stable 68-kDal peptide. An alternative explanation is that premature termination of transcription or translation could be occurring. . . . .

Adang '86 states that Example 12 "teaches the insertion of the full-length Bacillus thuringiensis insecticide gene between a T-DNA gene promoter and a polyadenylation . . . signal, the transfer of the insecticide gene to tobacco via a sub-Ti plasmid, the regeneration of plants containing the gene, and the expression of this gene under control of the T-DNA promoter in plant cells" (Adang '86, p. 62, first sentence of Example 12). While "Micro-ELISA double antibody sandwich assays were performed using a modification of the method of Example 7" (Adang '86,

p. 70, first sentence), it is not clear to what extent the ELISA assays indicated the presence of a toxic ~67 kD Bt crystal protein produced by tobacco cells transformed using a full length Bt crystal protein gene encoding Bt crystal protein of about 130 kD or a 130 kD Bt crystal protein. Adang Gene suggested in 1985 that "premature termination of transcription or translation could be occurring" (Adang Gene, p. 298, col. 2, second full para.). Because persons skilled in the art were well aware that Bt crystal proteins of about 130 kD and 68 kD are both toxic to Lepidopteran insects, Adang's toxicity test data does not establish that the regenerated tobacco plants of Example 12 produced a Bt crystal protein of about 130 kD in amounts insecticidal to Lepidopteran insects. Moreover, Adang '86 corroborates contemporary thought in the art that the results of assays widely used to identify the toxin produced by tobacco regenerated from tobacco plant cells transformed by a full length Bt crystal protein gene are both inconclusive and confusing (Adang '86, p. 75, last para.; emphasis added):

> Southern blot analysis of DNA isolated from presuptive [sic] transformants showed that cloned plant tissue having insecticidal activity in bioassays and containing crystal protein antigen generally had pH450's T-DNA. Northern blot analysis of RNA generally demonstrated the presence of mRNA having crystal protein sequences. These mRNA molecules were not the expected size of about 3.8 kbp, but

> were about 1.7 kbp in size. This was sufficient to encode the toxic portion if [sic] the crystal protein. As predicted from the fact that crystal protein levels in leaves as estimated by ELISA were below the limit of detection on western blots, western blot analysis of proteins extracted from transformed tissues did not reveal any antigens that cross-reacted with anti-crystal protein antibodies.

Based on the above evidence, we find that DeGreve's analysis, repeated below, most fairly reflects the state of the art on April 4, 1986 (DeGreve, p. 3, line 10, to p. 4, line 10; emphasis added):

> Although certain chimeric genes have now successfully been expressed in transformed plant cells, such expression is by no means straightforward. Various lines of evidence indicate that the level of expression of the foreign genes of non-plant origin not only varies greatly in different transformed tissues but are in general very low. Such low levels of gene expression could be due to several reasons: first, incomplete transcription of the gene resulting from inadvertent transcription termination signals; second, inefficient processing of the messenger RNA; third, impaired transport of the messenger RNA from the nucleus to the cytoplasm; fourth, instability of the cytoplasm messenger RNA; fifth, inefficient translation of the cytoplasm messenger RNA; and sixth, instability of the protein due to its susceptibility to plant specific proteins. Consequently, the successful transformation of plant cells using vectors . . . is not necessarily predictable prior to attempting a desired transformation.
>
> Engineering of differentiated plant cells and their progeny to express the Bt2 polypeptide and/or a truncated version thereof and/or polypeptide having substantial sequence homology thereto is far more difficult than other genes such as antibiotic resistance genes or other plant genes such as thaumatin due to one or more of the following: (1) the large size of the Bt2 toxin, even in its truncated form; (2) the particular

> properties of the Bt2 polypeptide (such as, but not limited to, solubility of the polypeptide); (3) the potential toxicity of the Bt2 polypeptide toward the plant cells; or (4) the Bt2 polypeptide synthesized in the plant cells and their progeny must retain substantially the same properties as the crystal protein synthesized in bacteria.

While Adang has presented the testimony and recent experimental evidence of persons said to be highly skilled in the art that the disclosures of both Adang 1983 and Adang 1986 would have enabled any person skilled in the art to make and use an embodiment of Count 1 without undue experimentation, we find that the views they express are necessarily influenced by experimentation performed after 1986 and knowledge acquired therefrom, i.e., hindsight. We emphasize that to obtain benefit of the filing date of an earlier filed application for subject matter defined by a count, the earlier application must enable persons skilled in the art to make and use an embodiment of the count as of the filing date of the earlier application. In order to be accorded benefit of the filing date of an earlier filed application, the original specification of the earlier filed application must satisfy the requirements of 35 U.S.C. § 112, first paragraph, for at least one embodiment of the count. Hunt v. Treppschuh, 523 F.2d 1386, 1389, 187 USPQ 426, 429 (CCPA 1975); Weil v. Fritz, 572 F.2d 856, 865-66 n.16, 196 USPQ 600,

608 n.16 (CCPA 1978). Enablement of an invention defined by the count is to be determined as of the filing date of the earlier application. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1387, 231 USPQ 81, 94 (Fed. Cir. 1987).

Weighing the testimony of Fischhoff's declarants and the results of the experiments they performed after 1986 against the testimony of Adang's declarants and the results of the experiments they performed after 1986, the balance on the issue whether Adang '86 would have enabled persons skilled in the art to make and use an embodiment of Count 1 at the time Adang '86 was filed neither favors nor disfavors patentability. However, because it is most consistent with essentially contemporaneous disclosures of the 1985-1987 publications discussed previously, including Adang's own 1985 publication (Adang Gene), we find the testimony and experimental evidence submitted in support of Fischhoff's view that the art was substantially unpredictable on April 4, 1986, more credible than the testimony and experimental evidence submitted by Adang's declarants.

The invention defined by Count 1 appears to be narrow. Nevertheless, the pertinent art of record and the art cited in Adang '86, indicates that, in April 4, 1986, the art of transforming live cells to express foreign genes was still

relatively new; published information was incomplete, misunderstood, and debated; and successes and failures were considered procedure-, DNA-, crop-, and pest-specific. In short, we find that the state of the art transforming live cells to express foreign genes on April 4, 1986, was highly unpredictable.

Accordingly, we find that undue experimentation would have been required to successfully transform living cells of tomato plants using full length Bt crystal protein gene/promoter constructs, regenerate living tissue from said transformed cells, and produce the full length protein encoded by the full length Bt crystal protein gene in said regenerated living tissue based on work with tobacco plants. We hold that to enable one skilled in the art to transform the living cells of tomato plants by a full length Bt crystal protein gene encoding a protein of 130 kd, persons skilled in art of transforming plant cells by foreign genes reasonably would have required the patent applicant's specification in support of the claimed subject matter to provide directions and/or guidance specific to tomato plants. The preponderance of evidence indicates that persons skilled in this art would have viewed general direction and guidance, i.e., no specificity or example, as inviting experimentation. In Adang '86, we find little, if any, guidance with regard to

transformation of tomato plant cells with a full length Bt crystal protein gene and regeneration of Bt insecticidal tomato plants therefrom. We find a single example wherein tobacco purportedly was regenerated from tobacco cells which, even when all the evidence is interpreted in a light most favorable to successful transformation thereof, constitutes questionable support for the tomato plant claimed. We are reminded that the word "tomato" appears but once in Adang '86, and there it appears in its plural form, "tomatoes". Adang '86 does include "tomatoes" in Table 2, a list of "Plants recommended for protection by B. thuringiensis insecticidal protein" (Adang '86, p. 87). However, the list also includes alfalfa, almonds, apples, artichokes, avocados, bananas, beans, beets, blackberries, blueberries, broccoli, Brussels sprouts, cabbage, caneberries, carrots, cauliflower, celery, chard, cherries, Chinese cabbage, chrysanthemums, citrus, collards, cos lettuce, cotton, cranberries, crop seed, cucumbers, currants, dewberries, eggplant, endive, escarole, field corn, filberts, flowers, forage crops, forest trees, fruit trees, garlic, grapes, hay, kale, kiwi, kohlrabi, lentils, lettuce, melons, mints, mustard greens, nectarines, onions, oranges, ornamental trees, parsley, pasture, peaches, peanuts, pears, peas, pecans,

peppers, pome fruit, pomegranate, potatoes, radishes, rangeland, raspberries, safflower, shade trees, shingiku, small grains, soybeans, spinach, squash, stone fruits, stored corn, stored grains, stored oilseeds, stored peanuts, stored soybeans, stored tobacco, strawberries, sugar beets, sugar maple, sunflower, sweet corn, sweet potatoes, tobacco, tomatoes, turf, turnip greens, walnuts, and watermelons (Adang '86, p. 87, Table 2; emphasis added). The complete list of plants includes fruits, vegetables, flowers, trees, grains, grasses, nuts, peppers, melons, spices, tobacco, etc., whether alive in the field or in storage. Among the plants listed are dicotyledonous plants, such as tobacco, which is known in the art for the comparative ease by which it can be transformed by foreign genes, and monocotyledonous plants, such as corn, feed grains, and grasses, which are known in the art for the unpredictability and uncertainty by which they can be transformed by foreign genes. See, for example, the court's discussion of the pre-1986 prior art cited in In re Goodman, 11 F.3d 1046, 1050-51, 29 USPQ2d 2010, 2013-14 (Fed. Cir. 1993). Id. at 11 F.3d at 1050, 29 USPQ2d at 2013, Goodman relates:

> Goodman's specification contains a single example of producing gamma-interferon in the dicotyledonous species, tobacco. . . . The specification does not contain sufficient information to enable the broad scope of the claims. For instance, production of peptides in

> monocotyledonous plants involves extensive problems unaddressed by Goodman's specification.

The Goodman court found that the prior art therein cited "shows great unpredictability in the art when Goodman filed the broad claims . . . in 1985." In re Goodman, 11 F.3d at 1051, 29 USPQ2d at 2014. Moreover, the court found, Id.:

> Goodman's own 1987 article . . . underscores the "major block" to using the claimed method with monocot plant cells. Goodman reports: "Although data have been cited that Agrobacterium can transfer T-DNA to monocotyledonous hosts, clear evidence of T-DNA integration exists only for asparagus, and, even in that case, no transformed plants have been described."

Thus, while Adang '86 suggests that plant cells of all of the plant types listed in Table 2 may be transformed by a Bt crystal protein gene encoding Bt crystal protein which is toxic to Lepidopteran insects and then regenerated into insecticidal plants with equal facility, persons skilled in the art having full knowledge of the state of the art in 1986 would not have understood that a description of a successful transformation of a cell of one plant from the list presented in Table 2 using a Bt crystal protein gene and regeneration of plants with insecticidal properties from that cell reasonably would have enabled one skilled in the art to transform a plant cell of any other species of plant from the list in Table 2 using a full length Bt crystal protein gene and regeneration of insecticidal plants from said

transformed other plant cell, with any reasonable expectation of success.

Adang provides an example (Adang '86, Example 12, pp. 62-75) which purports to establish that cells of at least one of the 94 kinds of plants recommended for protection by Bt insecticidal protein, namely tobacco, have been successfully transformed using a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD which is insecticidal to Lepidopteran insects. However, Fischhoff argues that Adang's example does not even establish that tobacco was transformed as described.[8]

To satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, it is not necessary for a patent specification to disclose, and preferably it omits, what is well-known in the

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[8] We notice the contradictory testimony of record on the issue whether Example 12 of Adang '86 shows that the tobacco plants therein bioassayed for insecticidal activity against Lepidopteran larvae were regenerated from tobacco cells which had in fact been transformed by a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD under control of a promoter such that said gene is expressible in said regenerated tobacco plant in amounts insecticidal to Lepidopteran insects. We fail to understand how the declarants can confidently assert that persons skilled in the art could have predicted success in transforming tomato plant cells and regenerating insecticidal tomato plants therefrom in 1986 in view of the apparent debate interpreting information disclosed in Examples 3, 4, and 12 of Adang '86. See, for example, the Declaration of Keith A. Walker Under 37 CFR § 1.132 (Adang '86, attachment to Paper No. 41 thereof) with respect to Example 12.

art. Hybitech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). However, as stated in Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997)(emphasis added):

> [T]hat general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

In our view, Genentech, Inc. v. Novo Nordisk A/S, supra, teaches that a specification requires persons skilled in an unpredictable art to perform undue experimentation to successfully make and use a claimed invention, even a narrowly claimed invention, when it provides no more than a general and/or nominal disclosure of starting materials, describes no more than general conditions under which a specific process of making and using an invention might be carried out, and includes not a single supporting example within the scope of the narrowly claimed invention.

At best, Adang '86 teaches that other kinds of plant cells, including the tomato plant cells of Count 1, might be transformed and regenerated in the same manner that tobacco cells can be transformed and regenerated.

In Senior Party Adang's Brief for Final Hearing, Adang specifically mentions the testimony of Drs. Cardineau, Walker, Schnepf, McCoy, and Stockhoff and summarizes their views on the question whether Adang '83 and '86 would have provided an enabling disclosure the subject matter described therein (AB, pp. 7, 19-20, and 24-27). Adang emphasizes the tomato plant regenerated from the cells Dr. Binns transformed in 1985 (AB, pp. 24-25, 27-28).[9] Adang criticizes the testimony and evidence provided by Fischhoff's witnesses, particularly Drs. Horst (AB, p. 26) and Perlak (AB, p. 28-29, 31-32). Adang specifically discusses the recent experimental evidence of Drs. Cardineau, Walker, McCoy, and Stockhoff in support of its assertion that Adang '86 was an enabling disclosure (AB, pp. 2, 30-31, 36-39). Adang acknowledges, however, that the testimonials of Drs.

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[9] Adang refers to the testimony provided by Dr. Binns and his staff relative to their efforts to transform tomato plant cells using a vector comprising a full length Bt crystal protein gene (AB, pp. 17-20). We consider Dr. Binns work in depth when we deal with Adang's case for earliest actual reduction to practice of an embodiment of Count 1.

Cardineau, Walker, McCoy, and Stockhoff are based on the results of experiments performed long after the filing date of Adang '86 and information not found in either Adang '83 or '86. For example (AB, pp. 38-39; footnote omitted; emphasis added):

> . . . Dr. Walker and Dr. McCoy testify that the recently conducted experiments demonstrate that tobacco, tomato and alfalfa can be successfully transformed with a binary vector and that tobacco can be transformed with a co-integrate vector (Walker Declaration) using the teachings of Adang's 1983 specification combined with the technology that was available in the art as of September 26, 1983. . . . .
>
> Where there were deviations from original protocols described by Drs. Cardineau's, Walker's, or McCoy's declarations in support of Adang's Motion No. 1 and Motion No. 4 Requests To Take Testimony On Experiments In Progress . . . the declarants explain why the changes were made and why the changes do not affect the validity of Adang's proof of enablement by Adang's 1983 application . . . .
>
> Declaration (A) of Brian Stockhoff is an expert declaration summarizing the bioassay results of the transformed plants made in recently conducted experiments. Dr. Stockhoff testifies that the recently conducted bioassays on tobacco, tomato, and alfalfa plants transformed with a full length *B.t.* are "compelling evidence of the successful expression of insect-controlling activity." . . . .
>
> In addition to submitting these four expert declarations, Adang also filed the declarations of 19 fact witnesses that helped conduct the various experiments.

We find that all experiments mentioned were recently performed, the declarants refer to technology available in the art as of

September 26, 1983, changes in experimental protocol had to be made, and 19 technicians were employed to perform the experiments.

Dr. Cardineau's views are based at least in part on experimentation performed and results achieved after Adang '86 was filed. We find that none of Dr. Cardineau's experimental results to which Adang points in his brief was reported in Adang '86. For example (AB, pp. 36-37):

> In an April 2, 1992 Declaration of Dr. Cardineau, Exhibits 4, 5, 6, and 7 show photographs of transformed tomato plants that have insecticidal activity . . . .
>
> Exhibits 5, 6 and 7 of Dr. Cardineau's Declaration demonstrate results of similar bioassays with insecticidal tomato plants. (AX-044) The plants of Exhibits 5 and 6 of Dr. Cardineau's Declaration were transformed with a full length *B.t.* gene, HD-73, whereas the insecticidal plant in Exhibit 7 was transformed with a truncated *B.t.* HD-1 dipel gene. In paragraph 17 of his declaration, Dr. Cardineau states that "all vectors were produced according to the teachings of the first application serial no. 535,354 and are exemplified in the pending [involved] application [Adang '92] at page 115 for Exhibit 4, pages 126 and 134 for Exhibit 5, and page 135 for Exhibit 6." (AX-044)
>
> . . . . .
>
> The April 2, 1992, declaration of Dr. Cardineau also includes evidence of insect resistance of potato plants transformed with the full length HD-1 dipel gene (Exhibit 9 of the Declaration), cotton plants transformed with the full length HD-73 gene (Exhibit 10 of the Declaration), and transformed sunflower tumors (Exhibit 11 of the declaration). (AX-044) According to Dr. Cardineau, each of these plants or tumors was produced using vectors made in

> accordance with the teachings of Adang's 1983 application at pages 20-81. (AX-044, para. 19-21)
>
> The April 2, 1992, declaration of Dr. Cardineau also includes evidence of a monocotyledonous plant, namely black Mexican sweet corn, transformed with a Coleopteran specific *B.t.* insecticidal protein gene vector. (AX-044, Exhibit 12) The transformation callus "was produced using methods of the invention according to the teachings of the first application at pages 20-81 to produce the vector for the transformation and the callus tissue resulting from the transformed plant cells." (AX-044, para. 22)[.]

Adang also acknowledges that the declarants relied on other information not presented in either of Adang's earlier applications (AB, pp. 37-38, bridging para.; emphasis added):

> There are four declarations of record, by four experts in the field, providing testimony that all of the working examples in Adang's later applications were conducted using methods and materials described in Adang's 1983 application combined with the knowledge of one of ordinary skill in the art as of September 26, 1983 filing date. (AX-280; AD-0497, AD-0519 and AD-1657) In these declarations, the experts explain in great detail where support in the 1983 application can be found or what pre-September 26, 1983 knowledge or publications could have been relied upon to carry out various steps of the methods.

As said in Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d at 1366, 42 USPQ2d at 1005:

> [F]ailure to meet the enablement requirement . . . cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement.

Here, as in Genentech, the specification invites further research. Adang '86 is an invitation to persons skilled in the art to experiment to determine if and how tomato plant cells can be successfully transformed by a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD and promoted to direct expression of the gene in tomato plant tissue regenerated therefrom and production of Bt crystal protein of about 130 kD by the regenerated tomato plant tissue in amounts which destroy or control Lepidopteran insects. It is fitting here to repeat the following statement taken from page 3, lines 26-29, of DeGreve's September 3, 1986, publication: "[T]he successful transformation of plant cells using vectors such as those described . . . is not necessarily predictable prior to attempting a desired transformation." We consider this statement and others referred to above to be of greater evidentiary value on this issue. The statements in the publications are more persuasive than the statements prepared especially for the proceeding. Cf. In re Carroll, 601 F.2d 1184, 1186, 202 USPQ 571, 573 (CCPA 1979).

Accordingly, we hold that the preponderance of evidence of record in this interference supports Fischhoff's motion under 37 CFR § 1.633(g) to attack the benefit of the April 4, 1986,

filing date, of continuation-in-part Adang '86, accorded Adang for the invention of Count 1 (Paper No. 23). Therefore, Fischhoff's motion is GRANTED. Accordingly, this interference is hereby

ORDERED REDECLARED with party Fischhoff newly designated Senior Party based on the benefit of the November 20, 1986, filing date of Application 06/932,818 accorded Fischhoff, and the October 21, 1988, filing date of Application 07/260,574 accorded Adang, for Count 1 in this interference as originally declared (Paper No. 2).

Fischhoff Motion No. 13

Fischhoff moves (Paper No. 25) under 37 CFR § 1.633(c)(2) to add new Claims 44, 45, and 46 (Appendix B) and have those claims designated as corresponding to Count 1. An APJ denied Fischhoff's motion in a decision mailed April 30, 1996 (Paper No. 121). 37 CFR § 1.637(c)(2) reads in pertinent part:

> A preliminary motion seeking to amend an application claim corresponding to a count or adding a claim to be designated to correspond to a count shall:
>
> (i) Propose an amended or added claim.
>
> (ii) Show that the claim proposed to be amended or added defines the same patentable invention as the count.
>
> (iii) Show the patentability to the applicant of each claim proposed to be amended or added and apply

> the terms of the claim proposed to be amended or added to the disclosure of the application . . . .

Fischhoff has not shown that proposed Claims 44, 45, and 46, all drawn to a chimeric gene comprising (1) a promoter which functions in plants, (2) a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD, and (3) a 3' non-translated region that functions in plants to cause the addition of polyadenylate nucleotides to the 3' end of an mRNA, wherein said promoter causes said Bt crystal protein to be expressible in a plant in an amount insecticidal to lepidopteran insects, are patentable to Fischhoff.

Claim 28 of Fischhoff '91, which is drawn to a chimeric gene comprising (1) a promoter which functions in plants, (2) a coding sequence which causes the production of mRNA encoding a crystal toxin protein of Bacillus thuringiensis, and (3) a 3' non-translated region which functions in plants to cause the addition of polyadenylate nucleotides to the 3' end of an mRNA, differs from proposed Claims 44, 45, and 46 solely with respect to the Bt coding sequence. The coding sequence of Claim 28 which causes the production of mRNA encoding a crystal toxin protein of Bacillus thuringiensis encompasses the full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD. We take particular note that Claim 28 stands rejected by an

examiner under 35 U.S.C. § 103 in view of prior art teachings of record (Fischhoff '91, Paper No. 19). Fischhoff's motion is DENIED.

Fischhoff Motion No. 14

Fischhoff moves (Paper No. 26) under 37 CFR § 1.633(f) for benefit of the November 20, 1986, filing date of Fischhoff '86 (Paper No. 26) for claims added in accordance with Fischhoff's motion to add new claims under 37 CFR § 1.633(c)(2)(Paper No. 25). An APJ dismissed Fischhoff's motion in a decision mailed April 30, 1996 (Paper No. 121). Since Fischhoff's motion under 37 CFR § 1.633(c)(2)(Paper No. 25) to add new Claims 44, 45, and 46 has been denied, Fischhoff's motion under 37 CFR § 1.633(f) is DISMISSED.

B. Adang's preliminary motions

Adang Motion No. 1

Adang moves (Paper No. 15) under 37 CFR § 1.633(f) to be accorded benefit of the September 26, 1983, filing date of Adang '83 for the subject matter of Count 1. The motion was deferred until final hearing by a decision of an APJ mailed April 30, 1996 (Paper No. 121, pp. 3-4).

We granted Fischhoff's motion under 37 CFR § 1.633(g) to attack the benefit of the April 4, 1986, filing date of

continuation-in-part Adang '86 accorded Adang for Count 1 (Paper No. 23). Since Adang '86 is a continuation-in-part of Adang '83, includes all of the disclosure thereof, and adds not only up-to-date information but also Example 12, and we have denied Adang benefit of its April 4, 1986, filing date, we also deny Adang benefit of the September 26, 1983, filing date of Adang '83 for Count 1, for the same reasons. Adang's motion is DENIED.

Adang Motion No. 2

Adang moves (Paper No. 16) for a judgment under 37 CFR § 1.633(a) that Claims 11-12, 15-16, 20-21, 24-25, 38-39, and 42-43 of Fischhoff '91, all claims in the involved application designated as corresponding to Count 1, are unpatentable under 35 U.S.C. § 102 and/or § 103. The motion was deferred until final hearing by decision of an APJ mailed April 30, 1996 (Paper No. 121, p. 4).

According to Adang (Paper No. 16, pp. 2-3, bridging para.):

> The Fischhoff claims are directed to a transformed tomato plant cell or an entire tomato plant regenerated from a transformed tomato plant cell. The tomato plant cell is transformed to comprise a full-length Bacillus thuringiensis (B.t.) crystal protein gene capable of encoding a Bacillus thuringiensis crystal protein of approximately 130-135 kD under control of a promoter such that the gene is expressible in the regenerated plant in amounts insecticidal to lepidopteran insects.

Adang's motion is based on a decision of the Board of Patent Appeals and Interferences in ex parte Appeal No. 91-0967 entered November 26, 1991 (Appendix A). The Board there affirmed an examiner's final rejection of Claims 1-9 and 37 of Fischhoff '86, the parent of involved Fischhoff '91, under 35 U.S.C. § 103 in view of the combined teachings of DeGreve,[10] Caplan,[11] Schnepf '036,[12] Schnepf,[13] and Adang Gene[14]. All claims stood or fell with finally rejected independent Claim 1 which read (Appendix A, Decision on Appeal No. 91-0967, pp. 1-2):

> 1. A method of producing genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larvae which comprises:
>
> (a) inserting into the genome of a tomato cell a chimeric gene which comprises

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[10] Vaeck et al. (DeGreve), European Patent Application 193,259, published September 3, 1986

[11] Caplan et al. (Caplan), "Introduction of Genetic Material into Plant Cells," Science, Vol. 22, pp. 815-821 (1983)

[12] Schnepf et al. (Schnepf '036), U.S. Patent 4,467,036, patented August 21, 1984

[13] Schnepf et al. (Schnepf), "The Amino Acid Sequence of a Crystal Protein from Bacillus thuringiensis Deduced from the DNA Base Sequence," The Journal of Biological Chemistry," Vol. 260, No. 10, pp. 6264-6272 (1985)

[14] Adang et al. (Adang Gene), "Characterized Full-Length and Truncated Plasmid Clones of the Crystal Protein of Bacillus thuringiensis subsp. Kurstaki-HD-73 and their Toxicity to Manduca Secta," Gene, Vol. 36, pp. 289-300 (1985)

(i) a promoter which functions in plants to cause the production of a mRNA transcript;

(ii) a coding sequence that causes the production of mRNA encoding a crystal protein toxin of Bacillus thuringiensis; and

(iii) a 3' non-translated region which functions in tomato to cause the addition of polyadenylate nucleotides to the 3' end of the mRNA;

(b) selecting transformed tomato cells; and

(c) regenerating from the transformed tomato cells genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larve [sic].

According to Adang, Fischhoff characterized the chimeric gene of Claim 1 on pages 2-3 of his Brief on Appeal in Appeal No. 91-0967 "as containing a coding sequence that causes the production of mRNA encoding a crystal protein toxin of Bacillus thuringiensis" (Paper No. 16, pp. 3-4, bridging sentence), i.e., mRNA encoding any Bt crystal protein toxin. Adang then notes that the Board affirmed the examiner's final rejection of Claim 1 of Fischhoff '86 under 35 U.S.C. § 103 in view of the combined prior art teachings and, in so doing, held (Paper No. 16, p. 4, citing the Decision in Appeal 91-0967, p. 7, line 13, to p. 8, line 2):

> DeGreve clearly discloses that the method disclosed in that reference which was successfully employed in tobacco plants in the working examples of the reference would be expected to work in a wide variety of other plants including vegetables. Reading the reference as a whole leads us to the conclusion that the ordinary skill in the art would reasonably expect a successful transformation of tomato plants with B.t. toxin gene in order to create insect resistant tomato plants. This is all that is required to reach a conclusion of prima facie obviousness.

Adang notes that Fischhoff thereafter filed involved continuing Fischhoff '91, presenting "claims directed to tomato plants and tomato plant cells per se, which were transformed by a full-length B.t. toxin gene" (Paper No. 16, p. 5). After first rejecting the new claims filed in Fischhoff '91 under 35 U.S.C. § 103 over the combined teachings of the same prior art applied in the rejection affirmed by the Board in Appeal No. 91-0967, the examiner "subsequently indicated that these claims were allowable" (Paper No. 16, p. 5).

Adang argues that the examiner's latest and continued holding that Fischhoff's new tomato plant and tomato plant cell claims corresponding to Count 1 are patentable over the previously applied prior art teachings is untenable. Hence, Adang filed this motion. Adang's motion is DENIED.

First, Claims 11-12, 15-16, 20-21, 24-25, and 38-39 of Fischhoff '91 all depend from either Claim 42 or 43. Claims 42 and 43 read:

> 42. A tomato plant which has been regenerated from a tomato plant cell transformed to comprise a full length Bacillus thuringiensis crystal protein gene capable of encoding a Bacillus thuringiensis crystal protein of approximately 130-135 kD under control of a promoter such that said gene is expressible in said plant in amounts insecticidal to Lepidopteran insects.
>
> 43. A tomato plant cell which is transformed to comprise a full length Bacillus thuringiensis crystal protein gene capable of encoding a Bacillus thuringiensis crystal protein of approximately 130-135 kD under control of a promoter such that said gene is expressible in said plant cell in amounts insecticidal to Lepidopteran insects.

Consistent with our interpretation of Count 1, we hold that both the transformed tomato plant cell, and tomato plant regenerated from the transformed tomato plant cell, of Fischhoff's Claims 42 and 43, both designated as corresponding to Count 1, must be transformed by a full length Bt crystal protein which encodes a Bt crystal protein of approximately 130-135 kD under control of a promoter which directs expression and production of Bt crystal protein of approximately 130-135 kD in said transformed tomato plant cell or tomato plant regenerated therefrom in amounts which destroy or control lepidopteran insects. We conclude that, unlike the "coding sequence that causes the production of mRNA encoding a crystal protein toxin of Bacillus thuringiensis" (emphasis added) which was used to transform the tomato plant cells of Claim 1 of Appeal No. 91-0967, the gene used to

transform the tomato cells of Fischhoff's Claims 42 and 43 is limited to a full-length Bt crystal protein gene which encodes a Bt crystal protein of approximately 130-135 kD, and the tomato plant cells transformed by said full length Bt crystal protein gene which encodes a Bt crystal protein of ~130-135 kD must express the full length Bt crystal protein gene and produce a Bt crystal protein of ~130-135 kD in amounts which result in the destruction or control lepidopteran insects. The distinction between the scope of the transforming genes is patentably significant for the following reasons:

(1) Fischhoff teaches (Fischhoff '86, p. 5, lines 9-33; emphasis added):

> The chimeric gene also contains a structural coding sequence which encodes the toxic protein of Bacillus thuringiensis or an insecticidally-active fragment thereof. It is known that Lepidopteran-type B. thuringiensis bacteria typically contains three toxin genes . . . . These genes are usually referred to as 4.5, 5.3 and 6.6 genes based on the size of the HindIII fragments obtained therefrom. It has been further shown that fragments of the complete toxin are insecticidally-active toward Lepidopteran larvae. Hence, for purposes of the present invention it should be understood that one can derive the coding sequence for an insecticidally-active toxin from any of the three genes and may further derive insecticidally-active fragments thereof without undue experimentation. Hence, for purposes of the present invention by "toxin protein" is meant either the full-length toxin as naturally produced by Bacillus thuringiensis or fragments thereof ("truncated toxin") possessing insecticidal activity toward the aforementioned Lepidopteran larvae. It has been found

that truncated toxin coding sequences are more easily expressed . . . .

(2) Fischhoff teaches (Fischhoff '86, p. 6, line 1, to p. 7, line 2; emphasis added):

> Those skilled in the art will recognize that promoters useful in a particular embodiment will necessarily depend on the stability of the mRNA transcript. Indeed . . . the truncated toxin coding sequences . . . appear to produce more stable mRNA transcripts which are more easily expressed. Accordingly, promoters that are not effective or less effective with full-length toxin coding sequences can often be used with truncated toxin coding sequences to produce an effective amount of toxin protein.
>
> . . . It should be understood that one may synthesize or isolate coding sequence encoding a toxin protein from one of the above-identified B.t. subspecies or others without undue experimentation and transform tomato plants to be toxic to susceptible Lepidopteran larvae as described herein. Accordingly, such variations and deviations are considered to be within the scope of the present invention. It should be further understood that the expression level may vary with the particular toxin coding sequence used and that the scope of toxicity toward Lepidopteran larvae may vary with the source of the toxin coding sequence (i.e. different B.t. subspecies).

(3) DeGreve teaches (DeGreve, p. 3, line 10, to p. 4, line 10; emphasis added):

> Although certain chimeric genes have now successfully been expressed in transformed plant cells, such expression is by no means straightforward. Various lines of evidence indicate that the level of expression of the foreign genes of non-plant origin not only varies greatly in different transformed tissues but are in general very low. Such low levels of gene expression could be due to several reasons: first, incomplete transcription of the gene resulting from inadvertent transcription termination signals; second, inefficient processing of the messenger RNA; third,

> impaired transport of the messenger RNA from the nucleus to the cytoplasm; fourth, instability of the cytoplasm messenger RNA; fifth, inefficient translation of the cytoplasm messenger RNA; and sixth, instability of the protein due to its susceptibility to plant specific proteins. Consequently, the successful transformation of plant cells using vectors . . . is not necessarily predictable prior to attempting a desired transformation.
>
> Engineering of differentiated plant cells and their progeny to express the Bt2 polypeptide and/or a truncated version thereof and/or polypeptide having substantial sequence homology thereto is far more difficult than other genes such as antibiotic resistance genes or other plant genes such as thaumatin due to one or more of the following: (1) the large size of the Bt2 toxin, even in its truncated form; (2) the particular properties of the Bt2 polypeptide (such as, but not limited to, solubility of the polypeptide); (3) the potential toxicity of the Bt2 polypeptide toward the plant cells; or (4) the Bt2 polypeptide synthesized in the plant cells and their progeny must retain substantially the same properties as the crystal protein synthesized in bacteria.

(4) Adang Gene teaches (Adang Gene, p. 298 (1985), col. 2, second full para.; emphasis added):

> E. coli pBT73-16 contains a complete crystal protein gene, yet peptides were observed ranging from the expected 133 kDal to 68 kDal. One explanation for this range in peptide sizes is that the translation product is not stable in E. coli but is proteolytically cleaved to a relatively stable 68-kDal peptide. An alternative explanation is that premature termination of transcription or translation could be occurring. . . .

(5) Vaeck consistently teaches (Vaeck, 328 Nature at 36-37; emphasis added):

> Four chimaeric genes containing modified Bacillus toxin genes under control of the 2' promoter of the Agrobacterium

TR DNA, have been transferred to tobacco plants. All contain the toxic core of the Bt2 protein; bt2 encodes the complete M_r 130K protoxin, bt884 is a 5' fragment of bt2 up to codon 610, Bt: neo23 and bt:neo860 encode fusion proteins which are relatively stable, both in bacteria and plants, and which retain full insect toxicity and NPTII enzyme activity.

Insecticidal levels of toxin were produced when truncated Bacillus genes or fusion constructs were expressed in transgenic plants. . . .

No significant insecticidal activity could be obtained using intact bt2 coding sequence, despite the fact that the same promoter was used to direct its expression. Intact Bt2 protein and RNA amounts in the transgenic plant leaves were 10-50 times lower than those for the truncated B. thuringiensis polypeptide or the fusion proteins. . . . Why the complete bt2 gene is not expressed at an equally high level in plant cells, is not known. Several parameters, such as differential RNA stability and translation efficiency might be important.

. . .

Our experiments illustrate the feasibility of engineering plants that defend themselves against lepidopteran insects which are sensitive to the B. thuringiensis berliner insect toxin. . . . To protect plants fully against these insects, higher levels of expression will be required. This might be achieved using chimaeric Bacillus genes containing stronger plant-specific promoters. The 35S promoter of cauliflower mosaic virus . . . for example directs a 10-50-fold higher expression than the regular T-DNA promoters in plants. Alternatively, it may be possible to construct chimaeric toxin genes with higher specific activity against important target insects. Transfer of different chimaeric genes into a variety of crops may provide a new and environmentally safer method of controlling destructive insect pests.

(6) Barton adds, "We eventually concluded that expression of intact δ-endotoxin[15] was lethal to plant cells" (Barton, 85 Plant Physiol. At 1105, col. 2, first para.).

The above-cited teachings as a whole convince us that the Board's decision in Appeal No. 91-0967 with respect to patentability under 35 U.S.C. § 103 in view of the applied prior art must be considered in light of the scope of the subject matter there claimed which includes transformation of tomato plant cells by "a chimeric gene which comprises (I) a promoter which functions in plants to cause the production of a mRNA transcript, [and] (ii) a coding sequence that causes the production of mRNA encoding a crystal protein toxin of Bacillus thuringiensis", i.e., any Bt crystal protein encoded by any Bt crystal protein gene, including truncated Bt crystal protein genes encoding Bt crystal proteins of significantly less than 130-135 kD. On the other hand, consistent with our conclusion that Adang '86 would not have enabled any person skilled in the art to make and use a tomato plant which has been regenerated from a tomato plant cell transformed to comprise a full length Bt

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[15] Barton states, "The crystal proteins, or δ-endotoxins, of *Bacillus thuringiensis* are lethal to Lepidopteran insects" (Barton, Abstract, l. 1-2).

crystal protein gene capable of encoding a Bt crystal protein of about 130 kD under control of a promoter such that said gene is expressible in said plant in amounts insecticidal to Lepidopteran insects, a conclusion which is supported by substantially the same art relied upon for obviousness in Appeal No. 91-0967, it is our view that Adang has not shown that Claims 11-12, 15-16, 20-21, 24-25, 38-39, and 42-43 of Fischhoff '91 are unpatentable to Fischhoff under 35 U.S.C. § 102 or § 103.

We conclude that none of the prior art references cited in Adang's motion would have enabled one skilled in the art to make and use the transformed tomato plant cells and/or tomato plants Fischhoff claims which produce Bt crystal protein of approximately 130-135 kD in amounts insecticidal to Lepidopteran insects without undue experimentation. To sustain a rejection under 35 U.S.C. § 102 over a single prior art reference, the reference must place at least one embodiment of the claimed subject matter in the possession of the public, i.e., the reference must have enabled one skilled in the art to make and use an invention claimed. Chester v. Miller, 906 F.2d 1574, 1576-77, 15 USPQ2d 1333, 1336 (Fed Cir. 1990); Akzo N.V. v. U.S. Int'l Trade Comm'n, 808 F.2d 1471, 1479, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986)(anticipatory reference must be enabling);

In re Donahue, 766 F.2d 531, 533, 226 USPQ 619, 621 (Fed. Cir. 1985)("prior art under 35 U.S.C. § 102(b) must sufficiently describe the claimed invention to have placed the public in possession of it"); In re Brown, 329 F.2d 1006, 1011, 141 USPQ 245, 249 (CCPA 1964); In re LeGrice, 301 F.2d 929, 936, 133 USPQ 365, 371 (CCPA 1962).

For unpatentability under 35 U.S.C. § 103, In re Dow Chem. Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988), instructs:

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art. . . . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure.

Accord In re Vaeck, 947 F.2d at 493, 20 USPQ2d at 1442. Here, as in Dow Chem. Co., 837 F.2d at 473, 5 USPQ2d at 1532, "[o]f the many scientific publications cited . . . none suggests that any process could be used successfully . . . to produce this product having the desired properties"; i.e., transformed tomato plant cells or plants which produce Bt crystal protein of approximately 130-135 kD in amounts insecticidal to Lepidopteran insects.

We find that prior art instruction relative to transformation of, and experimental success in transforming,

tomato plant cells using truncated forms of the full length Bt crystal protein gene under control of promoters which direct expression of truncated genes in tomato plant cells and tomato plants exhibiting insecticidal activity regenerated therefrom, would not have led persons having ordinary skill in the art reasonably to expect that tomato plant cells can be successfully transformed by a full length Bt crystal protein gene encoding a Bt crystal protein of ~130 kD under control of a promoter generally known to direct expression of a truncated gene, and that tomato plants which produce the full length Bt crystal protein in amounts insecticidal to Lepidopteran insects can be regenerated therefrom. Where, as here, the evidence indicates that there are significant differences in the sizes, structures, and properties of the Bt crystal proteins encoded by different segments of a full length Bt crystal protein gene and the various truncated gene sequences which encode each of those proteins reasonably would be expected to differ significantly, whatever preliminary expectation persons skilled in the art might have had of successfully transforming plant cells using a full length encoding sequence based on successful transformations using a truncated genetic code disappears. Consistent with the above view, Fischhoff states, "It has been found that truncated toxin

coding sequences are more easily expressed and, therefore, are preferred" (Fischhoff '86, spec., p. 5, lines 32-34; emphasis added). Consistent with DeGreve's teaching (EP 193,259, p. 3, l. 10, to p. 4, l. 10, published September 3, 1986), Fischhoff explains (Fischhoff '86, spec., p. 6, lines 1-11):

> Those skilled in the art will recognize that promoters useful in a particular embodiment will necessarily depend on the stability of the mRNA transcript. Indeed, . . . the truncated toxin coding sequences are preferred since they appear to produce more stable mRNA transcripts which are more easily expressed. Accordingly, promoters that are not effective or less effective with full-length toxin coding sequences can often be used with truncated toxin coding sequences to produce an effective amount of toxin protein.

Accordingly, Adang's motion is DENIED.

Adang Motion No. 3

Adang moves (Paper No. 17) under 37 CFR § 1.635 to have the teachings of Examples 3 and 4 of involved Adang '91, Adang '88, Adang '86, and Adang '83: (1) declared enabling to one skilled in the art, or in the alternative, (2) disregarded due to harmless omissions (Paper No. 17). The motion was deferred by decision of an APJ mailed April 30, 1996 (Paper No. 121, p. 4).

First, we are unable to consider the motion as presented on the merits. Adang has not clarified whether the applications are to be declared enabling under 35 U.S.C. § 112, first paragraph, with respect to (1) an embodiment of Count 1 relative to

Fischhoff's attack of the benefit accorded Adang of the April 4, 1986, filing date of Adang '86; (2) an embodiment of Count 1 relative to Adang's motion to be accorded benefit of the September 26, 1983, filing date of Adang '83; (3) the subject matter claimed in involved Adang '91; or (4) Adang's claims under 35 U.S.C. § 120 for benefit of the filing date of any one or more of his earlier filed applications for the full scope of subject matter defined by one or more of the claims in the involved application. Adang has the initial burden to show that its motion should be granted. 37 CFR § 1.637(a). Moreover, we have concluded that Adang '86 would not have enabled persons skilled in the art to make and use an embodiment encompassed by Count 1 for reasons unrelated to problems with Examples 3 and 4, whether any errors therein would have been apparent to persons skilled in the art or not. The motion is DISMISSED.

C. Fischhoff's motion to suppress

Fischhoff moves under 37 CFR § 1.656(h) to suppress certain evidence submitted by Adang in its case-in-chief (Paper No. 214, p. 1). "Except as otherwise provided in this subpart, the Federal Rules of Evidence shall apply to interference proceedings." 37 CFR § 1.671(b). Irrespective of this rule,

Fischhoff does not identify the Federal Rules of Evidence in support of its motion to suppress evidence.

Fischhoff argues that Adang has presented three types of objectionable evidence which should not be admitted (Paper No. 214, p. 8). The objectionable evidence includes:

(1) testimony and other evidence about the pH450 plant transformation vector as it relates to knowledge in the art prior the February 1985 date when, according to Fischhoff, the vector first came into existence;

(2) testimony and other evidence relating to protocols using the pH450 plant transformation vector and other protocols which, according to Fischhoff, are outside the scope of testing authorized by an APJ; and

(3) testimony and other evidence related to corporate enterprise from persons said to possess no direct and/or contemporaneous knowledge of work performed by the corporations on or about dates critical to the issues of enablement before us.

Federal Rules of Evidence, Article IV, Rule 401 (Pub. L. 93-595, Sect. 1, Jan. 2, 1975) reads:

> "Relevant evidence" means evidence having any tendency to make the existence of any fact that is of consequence to the determination of the action more probable or less probable than it would be without the evidence.

Rule 402 (id.) provides, "All relevant evidence is admissible, except as otherwise provided . . . ."

In this interference, Fischhoff questioned whether each of Adang's '88, '86, and '83 specifications would have enabled one skilled in the art to make and use an invention of Count 1 on its filing date. Any evidence which helps our understanding of the state of the art on or about any one of those dates is material to this case. Moreover, Fischhoff has thoroughly reported his view of the timeline for the plant transformation vector pH450 and the relevance of Adang's evidence to issues critical in this case. In that light, we properly admit the testimony and other evidence including Adang's use of the pH450 plant transformation vector as it relates to the issues whether Adang '88 and '86 would have enabled persons skilled in the art to make and use an embodiment of Count 1 and/or the full scope of subject matter of Adang's claims corresponding to Count 1 on their filing dates.

Similarly, even if Adang has parted from authorized experimental protocol and presented evidence related thereto, not only the results of the unauthorized testing protocol but the changes themselves are relevant to at least one critical issue in this case, i.e., whether persons skilled in the art would have been enabled to make and use an embodiment of the interference

count without undue experimentation. Moreover, unauthorized deviations in experimental protocol may be more informative on the issue of enablement than the experimental results. We will admit the testimony and other evidence. It is axiomatic that the evidence presented by the parties shall be considered for everything it shows. The deviations from authorized experimental protocol effect the weight of the evidence, not its admissibility.

Finally, both parties invite us to determine the state of the art as viewed by persons skilled in the art more than fourteen years ago. With this invitation in hand, it is best to consider all the evidence submitted by the parties relevant to the determination.

The objectionable evidence relates only to Fischhoff's motion 11 (Paper No. 23) to attack the benefit accorded Adang of the April 4, 1986, filing date of Adang '86, and Adang's motion 1 (Paper No. 15) to be accorded benefit of the September 26, 1983, filing date of Adang '83. Even considering and balancing all the aforementioned evidence, Fischhoff's motion 11 has been granted, and Adang's motion 1 has been denied. Therefore, the admissibility of this evidence is a moot issue. Accordingly, Fischhoff's motion to suppress evidence is DISMISSED.

5. Adang's case for priority of invention for Count 1

In Adang's Brief for Final Hearing, Adang argues (AB, p. 6):

> In its Brief for Final Hearing, Fischhoff alleges that it simultaneous conceived and actually reduced to practice a tomato plant within the scope of the Count on June 27, 1986. Fischhoff's alleged actual reduction to practice does not antedate the April 4, 1986, filing date to which Adang has been accorded benefit. Accordingly, Fischhoff's alleged actual reduction to practice does not entitle Fischhoff to judgment on the issue of priority.

Because we hold that Adang is not entitled to the benefit of the filing date of Adang '86 and, as a result, is the junior party in this interference, the burden shifts to Adang to show (1) actual reduction to practice of an embodiment of Count 1 prior to the November 20, 1986, filing date of Fischhoff '86, or (2) conception of an embodiment of Count 1 prior to the November 20, 1986, filing date of Fischhoff '86, coupled with diligence to a subsequent actual reduction to practice or constructive reduction to practice in the form of Adang '88 filed October 21, 1988. In its Brief for Final Hearing, Adang does not point to any showing of, or allege, priority based on the earliest date of conception of an invention of Count 1, coupled with diligence to actual or constructive reduction to practice. Accordingly, we look at the date Adang purports to have actually reduced an invention of Count 1 to practice.

Because Adang was initially accorded benefit of the April 4, 1986, filing date of Application 06/848,733, Adang criticized Fischhoff's evidence of an actual reduction to practice as follows (AB, p. 6):

> . . . Fischhoff's alleged actual reduction to practice does not satisfy several of the express limitations of the Count. For instance, Fischhoff did not prove that the genetic material used in the experiments encoded a B.t. crystal protein of about 130 kD. Likewise, Fischhoff did not prove that the putatively transformed plants expressed a B.t. crystal protein of about 130 kD. Fischhoff's failure to prove that the putatively transformed plants expressed any B.t. crystal protein is particularly egregious because Fischhoff also failed to prove that its alleged *B.t.* crystal protein gene was under control of a plant expressible promoter. A plant expressible promoter is essential to the invention of the Count because it determines whether the associated gene will be expressed in plants.
>
> The total lack of evidence of express limitations in the Count is fatal to Fischhoff's priority case, thereby limiting FISCHHOFF to its November 20, 1986, filing date.

Adang's criticism confirms (1) our holding that regenerated transformed tomato plants of Count 1 must not only express a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD, but the tomato plants must also produce Bt crystal protein of about 130 kD in amounts which destroy or control Lepidopteran insects; (2) our findings that plant cells transformed using a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD may express a

truncated form of the full length Bt crystal protein gene which encodes a Bt crystal protein of substantially less than about 130 kD and plant tissue regenerated from such transformed plant cells may produce Bt crystal protein toxin having a molecular weight substantially less than 130 kD in amounts sufficient to destroy or control Lepidopteran insects; and (3) our finding that production of Bt crystal protein of about 130 kD by plants regenerated from plant cells transformed using a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD in amounts sufficient to destroy or control Lepidopteran insects depends to a large extent upon the promoter selected to direct expression of the full length Bt crystal protein gene in the transformed plant cells from which the plants have been regenerated. Hence, Adang must not only show that he used a full length Bt crystal protein gene which encodes a Bt crystal protein of about 130 kD to transform tomato plant cells and regenerated tomato plants therefrom which produced a Bt crystal protein in amounts which destroy or control Lepidopteran insects, but Adang must show that the regenerated plants produced a Bt crystal protein of about 130 kD in amounts which destroy or control Lepidopteran insects.

In that light, we consider Adang's case for reduction to practice. Adang states (AB, p. 6, final para.; emphasis added):

> . . . Adang actually reduced to practice subject matter within the scope of the Count prior to Fischhoff's November 20, 1986, filing date. Adang transformed tomato plants with full length B.t. crystal protein gene in early 1985 and maintained the transgenic plants until 1986, at which time Adang conducted bioassays and observed insecticidal activity. Adang's work is fully described in a working example in Adang's 1988 application which, in its Brief for Final Hearing, Fischhoff concedes is a constructive reduction to practice of subject matter within the scope of the Count.

Adang directs us to look at the evidence of actual reduction to practice which is said to be "fully described" in working Example 15 of Adang '88 (Adang '88, pp. 144-56). Adang '88 introduces Example 15 as follows (Adang '88, p. 144):

> This Example teaches the expression in tomato (Lycopersicum esculentum) of the full-length Bacillus thuringiensis insecticide gene under control of both viral and T-DNA promoters.

Example 15.1 is labeled Leaf tissue transformation (Adang '88, pp. 144-45). Example 15.2 is labeled Hypocotyl transformation (Adang '88, pp. 146-47). Examples 15.1 and 15.2 describe general protocols for leaf and hypocotyl transformation. Example 15.3, labeled Transformations with Agrobacterium strains, describes tomato leaf and hypocotyl transformation efficiency (Adang '88, pp. 147):

> Hypocotyl transformations generally yielded higher efficiency of transformation as detected by octopine production and kanamycin resistance. Efficiency of leaf transformations varied in the range of about 0.5% to about 5.0% depending on the particular Agrobacterium strains while hypocotyl transformations ranged in efficiency from about 5 to about 40% (Table 12).
>
> Tomato plants were regenerated as described by Tatchell, S. and Bins, A. (1986) Tomato Genet. Coop. Rept. No. 36, pp. 35-36.

Example 15.4 describes ELISA protocols designed to detect total insecticidal protein in plant tissues (Adang '88, pp. 148-49). To that end, Example 15.4 utilized a "[p]rimary rabbit antisera against B. thuringiensis insecticidal protein" (Adang '88, pp. 148-49, bridging sentence). "Absorbances were read at 492 nm" (Adang '88, p. 149), i.e., Bt insecticidal protein absorbance read only at 492 nm does not distinguish between proteins.

Example 15.5 describes the protocol for detection of specific forms of B. thuringiensis insecticidal protein produced in transformed tomato plants using protein immunoblot procedures ("westerns")"(Adang '88, pp. 149-51). The reliability of the results from this procedure is criticized by Adang himself (Adang '88, p. 151; emphasis added):

> Extracts of control tissues were spiked with protoxin and/or toxin during extraction to estimate recovery during the western procedure. This showed that often insecticidal protein did not completely solubilize. As little as 0.01 ng

> of toxin was routinely detected on the blot. In 'spiked' samples, about 10 ng of standard was added to typical UC82 extract (from 100 mg tissue); the resultant signal on the blot represented about 30% recovery.

We find that the Example 15.6 Bioassays, aside from their questionable reliability, test for toxic Bt crystal protein produced by the plants, not how much 130 kD Bt crystal protein the plants produced (Adang `88, pp. 152-53; emphasis added):

> Bioassays were the most sensitive assay for the detection of Bacillus thuringiensis insecticide protein. Two types of bioassays were conducted on putative transgenic plants. In the first, the leaves were excised and placed in petri plates containing moistened filter paper. A predetermined number of first instar Manduca sexta (tobacco hornworm) larva were then added. . . . Substantial differences were observed between some varieties. However, results on a given R_0 or R_1 plant were not always consistent, due to either instability of insecticidal protein in excised leaves, or possible feeding of worms on moistened filter paper. In the second type of bioassay, first instar or, preferably, neonatal hornworms just hatched form [sic, from] . . . eggs were placed on plants in the greenhouse, and checked daily for growth and mortality after 7 to 9 days. Problems with this assay included worms leaving tomato plants and dying of desiccation due to high greenhouse temperatures ("wandering worms") and difficulties in finding hornworms on the tomato plants. These problems were adjusted for with control plant data, in which less than 20% mortality was consistently observed. "Wandering worms" were further controlled by placing the plants and worms in netted cages.

Example 15.7 reports that Southern and Northern blot nucleic acid analyses "were done" (Adang `88, p. 153). Standard techniques are said to have been employed.

Example 15.8 (Adang '88, pp. 153-56) reports the following RESULTS (emphasis added):

(1) Kanamycin-resistant tissues were obtained from all transformations. . . . R_0 plants from both pH578 and pH577 transformations . . . gave high octopine signals [Adang '88, p. 153];

(2) Two independent pH450 hypocotyl transformants yielded octopine-positive, G418-resistant tissues that regenerated plants containing octopine and B. thuringiensis insecticidal protein. Results from ELISA assays indicated insecticidal protein at levels ranging from 0.6 µg/g to 2.1 µg/g total protein. A substantial decrease in both total protein in the leaf and in insecticidal protein (µg/g total protein) was associated with plant age. Substantial degradation occurred, and in Western blots all ELISA-positive samples show smearing starting at about 110 kD [Adang '88, p. 154, first full para].

(3) ELISAs were used to screen putative transformants for high expression of Bacillus thuringiensis insecticidal protein. Detectable levels (greater than 5 ng insecticidal protein per g leaf tissue) were observed in transformed plants from pH450, pH577, and pH578, and R_1 plants of pH577 and pH582 transformations. All ELISA-positive plants tested killed some Manduca sexta larvae in bioassays (Table 13)[Adang '88, p. 154, second full para.].

(4) Western blots were used to determine the form of insecticidal protein expressed (protoxin or toxin) and to quantify the level of expression more precisely. In pH450 transformants, which contain the full-length Bacillus thuringiensis insecticidal protein structural gene, both protoxin and toxin was observed in leaf tissues. Tissues from pH577 and pH578 transformed plants also had both forms of the insecticidal protein. Different forms of insecticidal protein (protoxin and toxin) was [sic] also observed in different regenerated plants from what initially appeared to be a single

transformation event [Adang `88, pp. 154-55, bridging para.].

(5) Results for many of the plants assayed by bioassay are listed in Table 13. . . . Transformed plants from pH450 and pH577 gave the best biological activity. . . . [Adang '88, p. 155, first full para.].

(6) Southern analysis showed that insertions of T-DNA containing the plant-expressible insecticide gene were present in the expected organization, and are usually present in low copy number . . . . In all plants positive for protein and in bioassays positive plants tested, insecticidal protein sequences were observed in Northern blots of polyadenylated RNA. However, most of this mRNA was shorter than expected [Adang `88, pp. 155-56, bridging para.].

Next, we consider the time line and results described in Adang '88 as interpreted by Adang's Brief for Final Hearing (AB, pp. 17-18). According to Adang, "At the time Dr. Adang and Dr. Kemp developed their strategy to create transgenic insecticidal plants, their company (Agrigenetics) had already entered into a sponsored research agreement with the University of Pennsylvania and Dr. Andrew Binns" (AB, p. 17, first para.). In February 1984, Drs. Binns, Adang, Kemp and Merlo met and "arranged a collaborative project wherein personnel in Dr. Binns' laboratory would use vectors containing B.t. crystal protein gene, developed at Agrigenetics, to transform tomato plants and perform assays to evaluate the expression of the B.t. crystal protein gene in tomato plants (AD-0528)" (AB, p. 17, second

para.). According to Adang, the following ensued (AB, pp. 17-18; emphasis added):

> On March 28, 1985, Dr. Merlo provided Dr. Binns samples of the pH450 construct, which Dr. Binns understood to contain the full length B.t. crystal protein gene under control of the mannopine synthase promoter (the control of a plant expressible promoter) . . . .
>
> . . .
>
> In April, 1985, Dr. Binns initiated successful transformations of tomato plant tissue using the pH450 construct.
>
> On March 11, 1986, Dr. Binns initiated ELISA assays using samples from tomato plants transformed with pH450 and monoclonal antibodies for a B.t. crystal protein toxin (HD-73). On March 20, 1986, Dr. Binns determined that the tissue from plants transformed with pH450 were positive for the expression of B.t. crystal protein (AD-1476).
>
> In June 1986 Dr. Binns began sending Dr. Adang seeds from pH450-transformed tomato plants, and tissues from the transformed plants. (AD-0373, . . . AX-006 . . .). More seeds were sent in November 1986 from pH450 tomatoes . . . (AD-0396, . . . AX-006 . . .).
>
> On June 12, 1986, Dr. Adang received tomato tissues from Dr. Binns. These samples included leaf and stem tissues from plants that had been transformed with pH450. Dr. Adang appreciated that Dr. Binns had conducted bioassays on these tissues and observed insect toxicity. (AD-0373 . . .). Moreover, Dr. Adang appreciated that the full length B.t. gene contained in pH450 encoded a crystal protein toxin of about 130kD. [(AD-0373 . . .) and (AD-1479)] These plants constituted an actual reduction to practice of tomato plants within the scope of the Count.
>
> On October 23-29, 1986, Dr. Binns initiated additional bioassays of the transformed tomato plants from the pH450 hypocotyl transformation initiated on February 2, 1985.

> (AD-1486 to 1487, . . . AX-025 . . .) These bioassays were designed to test for B.t. insecticidal activity against Manduca sexta, the tobacco hornworm. The bioassays indicated that the B.t. protein was insecticidal in transformed tomato plants. These results were reported in Table 13 of Adang's 1988 application (AD-1486). This constituted another Adang actual reduction to practice of tomato plants within the scope of the Count before Fischhoff's November 1986 filing date.

When considering Fischhoff's showings, Adang argued that actual reduction to practice is not established until all the express limitations of the count are satisfied (AB, p. 6). Adang's view is consistent with precedent holding that an actual reduction to practice requires that the embodiment allegedly reduced to practice includes every limitation of the count. Schendel v. Curtis, 83 F.3d 1399, 1402, 38 USPQ2d 1743, 1746 (Fed. Cir. 1996). Therefore, to establish actual reduction to practice of an invention of Count 1 prior to the November 20, 1986, filing date of Fischhoff '86, Adang must prove that "the genetic material used in . . . [its] experiments encoded B.t. crystal protein of about 130 kD" and that tomato plants regenerated from tomato plant cells transformed by the genetic material used in the experiments produced Bt crystal protein of about 130 kD in amounts sufficient to destroy or control Lepidopteran insects (AB, p. 6).

In our view, the evidence shows that Adang transformed tomato cells using a pH450 vector which includes a full-length Bt crystal protein gene encoding Bt crystal protein of about 130 kD. However, to establish actual reduction to practice of an embodiment of Count 1 prior to the November 20, 1986, filing date of Fischhoff '86, Adang also must show that tomato plants regenerated from tomato cells said to be transformed by a full length Bt crystal protein gene encoding a Bt crystal protein of about 130 kD actually produced Bt crystal protein of about 130 kD in amounts sufficient to destroy or control Lepidopteran insects. Adang has not met his burden.

While the tests Adang, or his agents, are said to have performed before November 20, 1986, do indicate that "the putatively transformed plants expressed a B.t. crystal protein of about 130 kD" (AB, p. 6), they do not establish that B.t. crystal protein of about 130 kD was produced in amounts effective to destroy or control Lepidopteran insects. ELISA results indicated total Bt crystal protein, not Bt crystal protein of about 130 kD, i.e., ELIZA results indicate production of protoxin and/or toxin in all relative proportions. Kanamycin-resistant tissues and high octopine signals indicate that tomato plant cells had indeed been successfully transformed. However, the tomato plant cells

may have been transformed by the full length Bt crystal protein gene which encodes Bt crystal protein of about 130 kD and/or a truncated fragment thereof, any of which may carry the code for the marker. Thus, the ELISA results and identification markers do not establish that the full length Bt crystal protein gene was expressed by tomato plants regenerated from tomato plant cells transformed using a full length Bt crystal protein gene to produce Bt crystal protein of about 130 kD in amounts effective to destroy or control Lepidopteran insects.

The technical literature of record indicates that plants regenerated from plant cells transformed by vectors comprising a full length Bt crystal protein gene are likely to produce Bt crystal proteins of about 130 kD and about 68 kD, and may also produce Bt crystal proteins of about 106 kD and 50 kD (Adang Gene, p. 296 (Table II)). Adang '88 acknowledges that both forms of insecticidal protein (protoxin and toxin) were observed in tomato plants regenerated from tomato plant cells transformed using a full length Bt crystal protein (Adang '88, pp. 154-55, bridging para.; emphasis added):

> Western blots were used to determine the form of insecticidal protein expressed (protoxin or toxin) and to quantify the level of expression more precisely. In pH450 transformants, which contain the full-length Bacillus thuringiensis insecticidal protein structural gene, both protoxin and toxin was observed in leaf tissues. Tissues

> from pH577 and pH578 transformed plants also had both forms of the insecticidal protein. Different forms of insecticidal protein (protoxin and toxin) was [sic] also observed in different regenerated plants from what initially appeared to be a single transformation event.

Interestingly, for two independent pH450 Hypocotyl transformants yielding octopine-positive, G418-resistant tissues that regenerated plants containing octopine and B. thuringiensis insecticidal protein, "Western blots [of] all ELISA-positive samples show smearing starting at about 110 kD" (Adang '88, p. 154, first full para.), i.e., Bt crystal proteins having a molecular weights of 110 kD or less.

The prior art teaches that both the 130 kD and 68 kD Bt crystal proteins produced by plants regenerated from plant cells transformed by HD-73 vectors comprising a full length Bt crystal protein gene encoding a Bt crystal protein of about 130 kD are toxic to Lepidopteran insects (Adang Gene, p. 289, Summary, last sentence). The 68 kD toxin appears to be much less toxic than the 130 kD toxin (See Adang Gene, p. 290, col. 1, first full para.; p. 296, Table II; and pp. 297-98, bridging para.). However, Vaeck found (Vaeck, pp. 35-36, bridging para. et al):

> Plants transformed with the truncated bt2 gene . . . contain approximately ten times more Bacillus protein than those transformed with the complete bt2 sequence . . . . Thus, the failure to obtain insect-resistant plants using the intact bt2 gene is most probably due

> to inefficient protein synthesis in these transformed plant cells.
>
> Transgenic plants that express the shorter . . . protein are on the average more effective in killing insects and express higher levels of toxin than those expressing the longer . . . protein . . . .

Since the 130 kD and 68 kD toxins are both toxic to Lepidopteran insects, and Adang does not quantify the relative amounts of the Bt crystal proteins produced by the experimental tomato plants regenerated from tomato plant cells transformed by pH450, Adang's bioassays do not establish that the experimental tomato plants regenerated from the tomato plant cells Dr. Binns transformed produced Bt crystal protein of about 130 kD in amounts effective to destroy or control Lepidopteran insects. To the contrary, Adang's Western blots of ELISA-positive pH450 hypocotyl transformants are said to have shown smearing starting at about 110 kD (Adang 1988, p. 154, first full para.), i.e., 110 kD or less, and Southern analysis showed that most mRNA detected was shorter than expected (Adang '88, pp. 155-56, bridging para.).

Accordingly, we find that Adang's proofs that its pH450-transformed tomato plants and tissue from its pH450-transformed plants showed positive insect toxicity are insufficient to establish actual reduction to practice of a tomato plant within

the scope of Count 1. Adang's proofs do not show reduction to practice of tomato plants which produce Bt crystal protein of about 130 kD in amounts effective to destroy or control Lepidopteran insects. We do not agree with Dr. Binns's conclusions that the positive results of the October 1986 bioassays on tomato plants transformed by pH450 hypocotyl transformation reported in Table 13 of Adang '88 establish Adang's reduction to practice of tomato plants within the scope of Count 1 before Fischhoff's November 20, 1986, filing date.

Therefore, because party Adang has not shown by a preponderance of the evidence of record that it actually reduced an invention of Count 1 to practice prior to the November 20, 1986, filing date of Fischhoff '86, we conclude that Fischhoff is entitled to priority of invention for Count 1.

6. Disposition of Interference 103,324

This interference is decided based on the preliminary motions and the priority proofs submitted by the parties. Accordingly:

For Interference 103,324, it is

ORDERED that judgment on priority as to Count 1, the sole count in this interference, is awarded against party MICHAEL J. ADANG and JOHN D. KEMP;

FURTHER ORDERED that judgment on priority as to Count 1 is awarded in favor of party DAVID A. FISCHHOFF and STEPHEN G. ROGERS;

FURTHER ORDERED that, on the record before the Board of Patent Appeals and Interferences, party DAVID A. FISCHHOFF and STEPHEN G. ROGERS is entitled to a patent containing Claims 11-12, 15-16, 20-21, 24-25, 38-39 and 42-43 (corresponding to Count 1 of this interference) of Fischhoff Application 07/813,250, filed December 23, 1991; and

FURTHER ORDERED that, on the record before the Board of Patent Appeals and Interferences, party MICHAEL J. ADANG and JOHN D. KEMP is not entitled to a patent containing Claims 15-17, 22, 24-27, 29-32, 34, 40 (dependent upon Claims 16, 26, 27, 29, or 30), 42 (dependent upon Claims 16, 26, 27, 29, or 30), 43 (dependent upon Claims 16, 26, 27, 29, or 30), 44 (dependent upon Claims 16, 26, 27, 29, or 30), 46 (dependent upon Claims 16 or 26), 47-50, and 57 (corresponding to Count 1 of this

interference) of Adang Application 07/713,624, filed June 10, 1991.

It is also

ORDERED that if there is a settlement and it has not already been filed, attention is directed to 35 U.S.C. § 135(c) and 37 CFR § 1.661; and

FURTHER ORDERED that a copy of this decision be given an appropriate paper number and entered into the file records of Fischhoff Application 07/813,250 and Adang Application 07/713,624.

RICHARD E. SCHAFER)
Administrative Patent Judge)
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)
TEDDY S. GRON) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
) INTERFERENCES
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Interference 103,324

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